NHS

Screening Programmes

Sickle Cell and Thalassaemia

SICKLE CELL DISEASE IN CHILDHOOD

STANDARDS AND GUIDELINES FOR CLINICAL CARE

2nd edition October 2010

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Foreword

Sickle cell is the most common serious genetic disorder in England and as such it must be viewed as a mainstream issue for the National Health Service (NHS). It is estimated that about 350 babies are born each year in England with sickle cell disease and a further 9,500 babies are found to be carriers of the disease. The growing number of paediatric patients – many of whom come from disadvantaged communities in urban centres - require services at specialist level, local hospital level and community level which match those available for other conditions (such as cancer and cystic fibrosis) to foster health equalities and to provide a better quality of life for both the child and their family.

The first edition of these standards was warmly received when published four years ago. The importance of Transcranial Doppler (TCD) scanning for children with sickle cell disease to identify those at risk of stroke continues to be emphasised and it is now recommended that TCD scans be undertaken regularly on children from two years of age. Since 2006 various initiatives have been taken to ensure TCD is available to more children across the country: Guy's and St Thomas' Foundation Trust and King's College Hospital Foundation Trust have been commissioned to provide TCD training courses for healthcare professionals, standards and guidelines for TCD scanning were published in March 2009 (and are included in Appendix 10), and a quality improvement scheme is now being set up.

In 2008 the report entitled "A Sickle Crisis?" was published by the National Confidential Enquiry into Patient Outcome and Death. This report showed that, although clinical care for patients with sickle cell disease and thalassaemia has improved, there are still gaps in the service. Principal recommendations included the need for all healthcare professionals to have better training in and understanding of haemoglobinopathies, and for all patients to have access to clinical experts.

The support of Parliamentarians for sickle cell and thalassaemia patients led to the setting up of the All Party Parliamentary Group for Sickle Cell & Thalassaemia whose stated purpose is to reduce health inequalities by improving standards of care and by addressing other critical issues recommended by stakeholders. One initiative has involved discussions with relevant Royal Colleges to increase training on haemoglobinopathies for doctors and nurses.

Other initiatives to improve services include data collection and development of the National Haemoglobinopathy Registry so that patient numbers and case histories can be accumulated over time, thereby offering a comprehensive picture for commissioners to substantiate the need for clinical networks and services across the country. A peer review process has also been developed and delivered under the auspices of the UK Haemoglobinopathy Forum and the majority of paediatric specialist teams have been reviewed during the spring and summer of 2010.

We have now entered a period of new government and financial restraint with consequent change and uncertainty. It is hoped that the new arrangements for commissioning will include mechanisms for developing clinical networks as set out in the Specialised Services National Definition Set (included in Appendix 4). It is also hoped that there will be proper coordination of commissioning for both screening and care services so that every patient moves from screening to care along a seamless and comprehensive holistic pathway which includes medical care at all levels (specialist, local hospital and community) and full support services (including education, housing and welfare benefits) so that the quality of life is maximized for each patient and their family.

We share a great sense of satisfaction in seeing this second edition of the clinical standards being published; in particular that it has once again been the result of collaboration between clinicians, patients, the Sickle Cell Society and UK Forum on Haemoglobin Disorders, together with the Department of Health and the NHS Sickle Cell and Thalassaemia Screening Programme.

The Most Reverend & Right Honourable Dr. John Sentamu, Archbishop of York on behalf of the NHS Sickle Cell and Thalassaemia Screening Programme

Diane Abbott MP, Chair, All-Party Parliamentary Group

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Introduction: Aim of the document and revisions made October 2010

Sickle cell disease is now the most common serious genetic disorder in England, affecting over 1 in 2000 live births. The majority of cases occur in cities, where expertise and resources tend to be concentrated.[1] Nevertheless, with the introduction of universal newborn screening for sickle cell disease in England through the NHS Sickle Cell & Thalassaemia Screening Programme, implemented since 2006, affected infants have been identified in all parts of the country.[2] Sickle cell disease can therefore be regarded as a mainstream health issue in England.

This document sets out standards and guidelines for clinical care and recommendations for how care for children with sickle cell disease should be delivered.

The original standards and guidelines document was published as an "executive summary" in September 2006; detailed guidance and references were available only on the web. This document has now been revised to take account of updated information, and to incorporate relevant information from the detailed guidance along with other documents so that it is more comprehensive and should serve a wider readership which might include users & carers, nursing staff and commissioners as well as clinicians from both low and high prevalence areas.

Specific revisions to be noted include:

- Children with SCD should be offered annual TCD scans from aged 2 years (not 3 years as previously).
- Failsafe arrangements have been strengthened to ensure a more robust transition into clinical care services for all children with SCD as identified by the NHS Sickle Cell and Thalassaemia Screening Programme.
- A new standard has been included that requires data collection on all children with SCD; data should be submitted in a timely, accurate and comprehensive manner both to the NHS Sickle Cell & Thalassaemia Screening Programme and (directly consent is given) to the National Haemoglobinopathy Registry. Further details on data collection can be found in Appendices 7 and 8.
- Information contained in the "detailed guidance", including background information together with the rationale and evidence on which recommendations are based, has been incorporated into this document so that it is more comprehensive and may form a better learning and reference tool.
- Additional appendices have been added including, again to make the document more comprehensive :-
  - Appendix 4 – Specialised Services National Definition Set (3rd Edition) : Specialised Haemoglobinopathy Services (all ages) – Definition No.38;
  - Appendix 7 – Data collection by clinical networks to support monitoring of newborn outcomes;
  - Appendix 8 – National Haemoglobinopathy Registry;
  - Appendix 9 – Clinical peer review quality requirements;
  - Appendix 10 – Standards and Guidelines for TCD scanning for children with sickle cell disease;
  - Appendix 11 – List of sickle cell and thalassaemia centres nationally.

Please note that with reference to Appendix 10 - Standards and guidelines for TCD scanning - concerns have been raised regarding the lower cut-off points for high velocity/ high risk for TCD IMAGING. The following guidance note has therefore been added to the standards:

"The American STOP trial categories were based on non-imaging TCD and some studies have suggested that TCDi gives blood velocity values up to 10% lower. Therefore children with TDCi velocities >180cm/s but <200cm/s should be assessed very carefully for evidence of cerebrovascular disease. This may include frequent repeat TCD imaging, MRI/ MRA or repeat scanning with non-imaging TCD. Regular transfusion may be appropriate in this group if there is evidence of established or progressive cerebrovasculopathy or other neurocognitive concerns. The course of action in these cases must be decided by the clinicians responsible for the clinical care, taking into account individual circumstances and the diagnostic facilities available.

Further work is being undertaken to resolve the apparent discrepancies between the velocities measured by imaging and non-imaging TCD scanning and to harmonise the results from the two techniques."

In this revised document, the term "Specialist Haemoglobinopathy Teams" (SHT) has been used to replace "Sickle Cell Centre" and the term "Local Haemoglobinopathy Teams" (LHT) has been used to describe local hospital teams. The terms SHT and LHT are also used in the quality requirements used in the peer review process.

These guidelines have been written to support responsible clinicians and to ensure that every infant has access to the same quality of care wherever they live. They are written primarily for paediatricians and haematologists working in local hospitals (LHTs) rather than for specialist haemoglobinopathy teams (SHTs) and propose standards that can be monitored by hospital trusts and commissioning authorities. They refer where relevant to other related standards, e.g. the newborn screening programme (see Appendix 3), National Service Framework for Children guidance[3] and National Service Frameworks for chronic disease management in adults based on models from the USA.[4,5] Standards for the care of adults with sickle cell disease have been published by the Sickle Cell Society.[6]

The document is not intended to provide extensive clinical guidelines for the management of acute complications. There are many such guidelines, mainly from the USA. Some of these are tailored to the UK experience, such as *Guidelines for the management of the acute painful crisis in sickle cell disease*[7]. Note that the management of pain is currently being reviewed by NICE and revised guidelines are expected to be published in the near future.

A clinical network of local and specialist hospital teams (LHTs and SHTs) has been proposed for some time but, in most cases, these networks have not yet been formally designated by commissioners and there is no infrastructure to support the functioning of the networks; they therefore remain as informal arrangements between local hospitals, clinicians and commissioners. Recommendations to develop the networks more formally were included in the report commissioned by the Department of Health[8]. The concept of three levels of care was also recognised in the Specialised Services National Definition Set (see Appendix 4) which sets out care to be provided by specialist teams, local teams and community teams. In both these models it is envisaged that care will be provided locally wherever possible, but that SHT will develop protocols with local units for treatment of acute complications, and for referral where necessary. Networks and SHT centres are included in Appendix 6.

This document outlines a model of care for children with sickle cell disease who have been identified through the newborn screening programme. It extends from newborns until transition – which is usually between 16 and 18 years. It will also have relevance for the care of children who may have missed out on newborn screening before the programme was introduced, or who have come from abroad and been diagnosed after the newborn period. It is based on a consensus of clinicians with experience in the UK, Jamaica and the USA.

Recommendations are graded as follows (based on Agency for Health Care Policy & Research recommendations):

A
(levels 1a, 1b)
Requires at least one randomised trial as part of the body of literature of overall good quality and consistency addressing the specific recommendations.

B
(levels 1a, 1b, 1c)
Requires availability of well-conducted clinical studies, but no randomised clinical trials, on the topic of the recommendations.

C
(level IV)
Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

References

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Sickle cell disease in childhood

Conditions to be treated

Sickle cell disease (SCD) denotes all genotypes containing at least one sickle gene in which HbS makes up at least half the haemoglobin present. In addition to sickle cell anaemia (**HbSS**) there are other compound heterozygous conditions which occur in the UK. Conditions to be treated:-

Haemoglobin SS
Haemoglobin SC
Haemoglobin SD^{Punjab}
Haemoglobin SE
Haemoglobin S/ß thalassaemia (ß+, ß^0, δß and Lepore)
Haemoglobin SO^{Arab}

Haemoglobin S/HPFH (Hereditary Persistence of Fetal Haemoglobin) is indistinguishable on neonatal screening from HbSS or Hb S/ß^{0}thalassaemia. Family studies and DNA testing may clarify the diagnosis. HbS/HPFH is not thought to cause clinical complications and there is no evidence as to whether children with this should be followed up regularly. There is no evidence that they develop splenic hypofunciotnn and prophylactic penicillin is not recommended.

Incidence, prevalence and survival

SCD is now the most common serious genetic condition in England, affecting more than 1 in 2,000 live births. The birth prevalence in some urban areas may be as high as 1 in 300.[1] It is found at a low frequency in all populations, the highest prevalence occurring in people of African and African-Caribbean origin. Cases also occur in families originating from the Middle East, India and the eastern Mediterranean.

Life expectancy has improved considerably over the last decades due to improved recognition and better management of acute episodes. Introduction of neonatal screening programmes in parts of the USA dramatically improved healthcare, and childhood mortality is now about 1-2%[2] in some areas. Where programmes have been introduced in the UK, a similar benefit has been seen.

However, in the USA there is a marked geographic difference in mortality of young children with sickle cell disease which greatly exceeds mortality of black children without the disease.[3,4] This highlights the importance of having a robust follow-up programme and access to high-quality care wherever a child with SCD lives.

A US multicentre study in 1994 reported a median survival in sickle cell anaemia of 42 years in men and 48 years in women; and for haemoglobin SC disease, of 60 years and 68 years respectively.[5] Survival estimates for sickle cell anaemia in Jamaica based on a clinic population suggested median survival for men of 53 years and 58.5 years for women.[6] Life expectancy in the UK is not known, but is likely to be similar.

Pathophysiology

A single nucleotide substitution in the sixth codon of the ß globin gene results in the substitution of valine for glutamic acid on the surface of the variant ß-globin chain. This change causes HbS to polymerise when deoxygenated, the primary event in all sickle cell pathology.

Polymerisation is dependent on intra-erythrocytic HbS concentration, the degree of haemoglobin deoxygenation, pH and the intracellular concentration of HbF. The polymer is a rope-like fibre that aligns with others to form a bundle, distorting the red cell into characteristic sickled forms.

These deformed sickle red cells can occlude the microvascular circulation producing vascular damage, organ infarcts, painful episodes and other symptoms associated with SCD.

There are two essential pathological processes: haemolysis and vaso-occlusion.

- Haemolysis results in anaemia and a functional deficiency of nitric oxide which results in vascular endothelial damage and may be responsible for complications such as pulmonary hypertension, priapism and stroke.
- Vaso-occlusion causes acute and chronic ischaemia and is responsible for acute pain and organ damage.

A recent review gives a comprehensive account of the current understanding of pathophysiology in sickle cell disease[7].

Presentation

There is a wide range of clinical presentation and severity. In the unscreened population, infants may present with sudden death from pneumococcal sepsis due to splenic hypofunction, or acute splenic sequestration, before a diagnosis is made. Dactylitis is a common presenting symptom in infants between 9 and 18 months, but many children do not experience this and may only present after 2 years with vaso-occlusion affecting the long bones.

Painful episodes due to vaso-occlusion are the most common complications and account for the majority of hospital admissions, although SCD can affect any organ in the body. Strokes affect 5-10% of the paediatric population and, in addition, there may be MRI changes of silent stroke in up to 20% of the affected population before the age of 20 years. These children may experience cognitive problems or difficulties with psychological adjustment. Acute chest syndrome – which may be precipitated by infection, infarction or a combination of the two – is another serious cause of morbidity and mortality. Other complications include lung damage, hepatobiliary disease, renal disease, osteomyelitis, avascular necrosis, eye complications, priapism and leg ulcers.

Variability

Some children with SCD are severely affected, while others remain symptom-free. This variability is not completely understood but is partly due to the presence or absence of secondary effector genes that participate in some of the pathological events related to vaso-occlusion. The fetal haemoglobin (HbF) level is constant throughout life (after stabilisation during infancy) and is a relatively good predictor of disease severity[8].

Concurrent α-thalassaemia carrier status is also thought to affect severity, but the evidence is conflicting as the beneficial effects of higher haemoglobin may be outweighed by increased viscosity. Consequently avascular necrosis and proliferative retinopathy occur more frequently in sickle cell patients with α-thalassaemia trait. However, stroke is less common and there seems to be no overall effect on life expectancy.

Haemoglobin SC disease

Although all the same complications of HbSS may occur in haemoglobin SC disease, the latter is often a much milder condition. In the absence of a screening programme it may not be detected until adulthood or a chance blood test. It accounts for half the number of acute episodes of pain compared to HbSS, and there is also less likelihood of splenic hypofunction.

References

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Delivery of healthcare

SCD represents a unique challenge in the UK. An equitable and comprehensive care programme for children with these conditions must take into account the wide geographical variation in prevalence, combined with the known variability in the severity of sickle disorders. Any service planned for these disorders must deliver both an optimal level of care close to the patient's home and access to an SHT. In addition, services should support parents and carers to manage the condition at home where appropriate.

As SCD becomes more common across the UK, every hospital should be able to provide basic inpatient and outpatient care for local patients and all hospitals which have an emergency department and/or acute paediatric unit should be able to provide emergency care of acute sickle problems, most commonly severe pain. However, children with this chronic condition should also have the benefit of specialised knowledge. The development of a network of LHTs supported by SHT centres has been accepted as an appropriate way to provide high-quality, long term care across England.

Community care

Until recently, SCD has been managed almost exclusively in acute hospitals. This has partly been due to SCD being seen as a specialised condition of which general practitioners may have little knowledge or training. In addition parents are often quite knowledgeable about their child's condition and will know when home treatments are not working or when an emergency necessitates them taking their child straight to hospital.

In general, parents need to be encouraged to use primary care more often. Practical information needs to be given to the general practitioner such as dosages of medications, steady state values, as well as the information that has been given to parents about the condition and ways of accessing hospital care.

In areas of high prevalence there may be sickle cell and thalassaemia community centres that provide an information resource, support and advice to families, training for health and other professionals as well as genetic counselling and specialist nursing. For a list of centres, please see Appendix 11.

Local authority services for SCD are not well developed. Patients with SCD, unless they have a chronic disability such as stroke, do not fulfil the disability criteria for acceptance by social services departments. This is despite the fact that frequent acute exacerbations disrupt normal life and may be as disabling as other chronic conditions. Similarly, education authorities do not monitor children with SCD unless the child has been found to have a learning disability and has special educational needs. There is a need to inform these professionals that overt or silent stroke can often cause cognitive impairment that leads to learning difficulties. (This occurs in about 20% of affected children and young people under 20 years). These acquired impairments may be missed in children who started their school career without any difficulties.

SCD should be considered as a chronic illness with acute exacerbations that have far-reaching effects on education, family life, social integration and the emotional wellbeing of the child and family.

When organising care, it will be important to take into account local community support and health provision, including child and adolescent mental health services (CAMHS), education, social services and self management as well as hospital care. Training for general practitioners, community nursing and local authority employees will be needed, along with inter-agency agreement on criteria for referral to social services and education for support.

Current policy promotes a chronic disease model for the management of conditions such as SCD. Its main components have been constructed after a literature review and evidence from a panel of experts in the USA[1]. This model relates mainly to adults.

In the UK, community paediatricians already have extensive experience in coordinating community services and liaising with education, social services, the voluntary sector, CAMHS and the acute sector. Community paediatricians could therefore be key in setting up clinical networks for this group of children as recommended in the National Service Framework guidance for children and young people who are ill[2]. Such networks include:

- Comprehensive and integrated local services recognising that children are best cared for at home whenever possible;
- Managed local children's clinical networks (LHT) taking into account the particular needs of the group, geography and transport arrangements.

Table 1 Roles and responsibilities for community services (as of 1 January 2010)

Organisation	Responsibilities
NHS	
Primary Care Trust	Commissioning of acute and community medical services, including child and adolescent mental health services. Expert Patient Programme.
GPs	Register details from newborn screening programme. Prescribe penicillin as appropriate. Provide primary care for common childhood illnesses. Be aware of signs and symptoms that need emergency hospital assessment. Prescribe analgesics in conjunction with paediatrician.
Practice nurse	Administer conjugate pneumococcal vaccine at 2, 4 and 13 months (as per routine immunisation programme) + annual flu. Undertake treatments as appropriate, e.g. dressing of leg ulcers.
Health visitor	Routine health promotion advice and screening. Targeted visits (following local guidance for child in need). Link with specialist nurse counsellor where available.
School nurse	Routine health promotion advice and screening Liaison with school staff re extra needs of children and awareness of symptoms and signs Link in with specialist nurse counsellor where available
Community paediatrician	Liaison with local authority (social services and education) re needs of child. Assessment of children with developmental delay. Coordination of community services in cases of chronic disability, e.g. stroke. Maintenance of disability register in conjunction with local authority.
Specialist nurse counsellor/nurse practitioner (may be employed by acute trust)	Specialist support to families. Training and support of community nurses. Liaison with primary care and hospital services. Support of care in the home.
Child and adolescent mental health service (CAMHS)	Provision of clinical psychology assessment and management Provision of neuropsychology services
Local Authority	
Education	Regular awareness training for school staff. Early recognition of child with acquired learning difficulties, e.g. from silent stroke. Support for child identified with learning disability or with chronic health problems impacting on education. Assessment by educational psychologist.
Social services	Recognition of child as "child in need". Registration on Children's Disability Register. Respite where appropriate.
Voluntary sector	Provision of information about condition and local resources, support and respite for families. Provision of advocacy services. Facilitation of service user feedback and engagement.

Specialist haemoglobinopathy care

The model of local and specialised centres is well established for the treatment of such conditions as cystic fibrosis, cancer and haemophilia. The value of haemoglobinopathy centres has been well documented in the USA.[3]

Two broad categories of sickle cell centres are proposed:

- Hospitals in urban areas with a large local population of children with SCD. These should have appropriate experience, staffing and facilities.
- Hospitals in low prevalence areas with few local patients, but where geography dictates that they will need to provide most services for sickle patients. These would act as a centre of expertise for patients in the surrounding areas. They are generally large district general or teaching hospitals which accept referrals for acute and outpatient care from other hospitals or regions.

In both cases, it may be necessary to refer to a tertiary/specialist centre for certain services such as urology and intensive care. In many areas informal networks and referral patterns exist. In this case, the initial aim is to formalise these arrangements and establish a network of centres across the country (see Appendix 6 for list of network of centres).

Definition of specialist haemoglobinopathy team (SHT)

SHTs and centres should fulfil the following criteria:

- Have a designated paediatrician/paediatric haematologist/haematologist with a specific interest in paediatric haemoglobinopathy.
- Have a designated paediatric haemoglobinopathy clinic (which may be part of a larger clinic).
- Provide paediatric high dependency and intensive care, or have established protocols for the referral of patients to a hospital with paediatric HDU/ICU with experience and protocols for the management of SCD in children.
- Have CPA-accredited laboratory facilities for accurate haemoglobinopathy diagnosis.
- Have established links with local neonatal screening programme and sickle cell counsellors.
- Have access to Transcranial Doppler (TCD) scanning.
- Have links with clinical psychology for specialised treatment and neuropsychometric assessment.
- Participate in peer review process. See Appendix 9 for further details.

Role of SHT

- Develop shared care arrangements with local hospitals and, where appropriate, provide outreach clinics in local clinics.
- Support and promote management at home.
- Have shared protocols and facilities for the treatment of acute complications, e.g. acute pain, acute chest syndrome, stroke, acute anaemia, acute splenic sequestration, priapism
- Provide expert in-patient care for acute complications of SCD.
- Provide and organise the management of chronic complications:
  - Monitoring and screening for neurological complications including TCD ultrasonography.
  - Monitoring regular blood transfusion therapy, including iron stores, iron chelation and secondary effects of iron overload.
  - Initiation of hydroxyurea (hydroxycarbamide), long-term transfusion therapy or bone marrow transplantation.
- Provide a clinical psychology service.
- Carry out an annual review of all children.
- Maintain a list of all children to monitor outcome and quality of follow-up.
- Develop links with other specialists who need to be involved, e.g. community paediatricians, ENT, anaesthetics, orthopaedic and paediatric surgeons, dentists, neurologists, ophthalmologists, paediatric urologists.
- Take part in transition plan to the adult service.
- Provide training for students, doctors and nurses.
- Carry out audit and research.
- Provide an appropriate referral pathway for HSCT (i.e. bone marrow/stem cell transplant).
- Advise on all surgical procedures occurring within the network.
- Provide accurate, comprehensive and timely data to the NHS Sickle Cell and Thalassaemia Screening Programme to enable outcomes of newborn screening to be evaluated – refer to data collection required set out in Appendix 7.
- Complete and update entries into National Haemoglobinopathy Registry (when consent has been given) – refer to information in Appendix 8.

Local hospital care

The local hospital and LHT should:-

- Have a named paediatrician to link in with SHT and neonatal screening laboratory.
- Arrange initial contact with family and provide a paediatric clinic for routine outpatient management.
- Promote and support management at home by parent, GP and community sickle cell and thalassaemia centre (if available).
- Manage acute pain and acute anaemia and provide initial care for other complications before transfer to the SHT according to shared guidelines and protocols.
- Liaise with SHT for annual review.
- Follow up children who fail to attend, reporting to SHT on annual activity as part of a network review meeting.
- Liaise with local authorities, e.g. education and social services.
- Manage transition to the adult service.
- Provide accurate, comprehensive and timely data to the NHS Sickle Cell and Thalassaemia Screening Programme to enable outcomes of newborn screening to be evaluated – refer to data collection requirements given in Appendix 7.
- Complete and update entries into National Haemoglobinopathy Registry (when consent has been given) – refer to information in Appendix 8.

Table 2
Roles and responsibilities of acute care

Acute NHS trusts (LHTs)	Network of local hospitals and SC&T specialist network centres (SHTs)
Accident & emergency	Access to guidelines for ambulance staff. Protocols for assessment and management of children who present as an emergency. Protocols for transfer
Outpatients	Protocols for investigations and treatment. Protocol for managing non-attenders. Communication with GP and Health Visitor/School Nurse. Ongoing support for family and promotion of care in the home.
Paediatric/surgical wards	Protocols for acute management. Links with local PICU. Protocols for transfer.
PICU	Protocols for intensive care of sickle cell complications.

Table 3
Staffing resources required

Staffing and resource recommendations	Local unit (LHT)	SC&T specialist network centre (SHT)
Designated paediatrician	x	
Designated paediatrician and/ or haematologist providing a lead for the service		x
Named deputy for each	x	x
Middle-grade cover (SpR/staff grade) available out of hours	x	x
Named paediatric nurse	x	
Specialist nurse in SCD		x
Access to clinical psychology	x	

Staffing and resource recommendations	Local unit (LHT)	SC&T specialist network centre (SHT)
Clinical psychologist with an interest in sickle cell disease and/or neuropsychologist		x
Appropriate laboratory support (transfusion, haemoglobinopathy testing and other)	x	x
Access to MRI, CT and PICU		x
Administration for support of clinics and maintaining local lists of children attending	x	x
Transcranial Doppler service		x
Link with bone marrow transplant service		x
Access to paediatric neurology		x
Access to paediatric endocrinology		x
Access to paediatric ophthalmology		x
Access to paediatric orthopaedics		x
Links with adult service for SCD	x	x

Recent peer reviews reveal very wide discrepancies in staff resources across different units. The areas most affected are medical and specialist nursing provision together with Psychology support. Some variation in staffing is inevitable as it will depend on other factors such as number of available supporting staff and case mix . However an expected minimum requirement might be: one WTE consultant paediatric haematologist (or paediatrician with expertise in Haemoglobinopathy disorders), one WTE specialist nurses, and one WTE psychologist for every 200 patients with a major haemoglobin disorder based at any centre . Further work and recommendations arising from the peer review process should be available at the end of 2010 which may give more detail on specific areas of need and inform the setting of minimum staffing requirements.

Shared care

Shared care arrangements will vary according to local needs and circumstances. It may be appropriate in some areas for the specialist team (SHT) to visit the local unit and in others for children and their families to travel to the SHT centre.

Provision of PICU/HDU

Some of the proposed SHT centres and many of the local hospitals do not have provision for PICU/HDU or MRI scanning. Arrangements will need to be made to develop shared protocols with regional paediatric and PICU units for the assessment and management of acute neurological complications, for exchange transfusions in an acutely unwell child and for children needing ventilatory support.

Provision of Transcranial Doppler ultrasonography

Annual TCD ultrasound assessment of children with SCD from the age of 2 years is recommended. This is based on the findings of a randomised controlled trial on the benefits of transfusion in children with raised cerebral blood-flow velocities[4].

The NHS Sickle Cell and Thalassaemia Screening Programme has published standards and guidelines for Transcranial Doppler scanning in children with SCD (see Appendix 10). All children and young adults with SCD (Hb SS) and Hb S/ß0 thalassaemia should be offered annual TCD scans from age 2 years until at least 16 years. The need for children with other types of SCD to be tested should be reviewed on a case-by-case basis.

Most of the proposed SHT centres have now developed TCD scanning for children with SCD or have strong links and referral systems to other specialist centres. Supervision of this TCD programme is the responsibility of the SHT.

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Audit Standards

These proposed standards are based on current evidence-based practice, accepted good practice and knowledge of current resources.

Penicillin prophylaxis

i) 90% of infants should have been offered and prescribed Penicillin V (or alternative) by 3 months.

ii) 99% of infants should have been offered and prescribed Penicillin V (or alternative) by 6 months.

iii) Any parental refusal should be documented.

Pneumococcal immunisation*

i) 95% should be given Pneumovax (polysaccharide antigen) at 2 years of age (24-27 months) and five-yearly thereafter.

TCD scanning

i) 90% of children with SCD (Hb SS and HbS/β0 thalassaemia) should be offered annual TCD scans from the age of 2 to 16 years by 2012.

ii) 99% of SHT centres should have the capability of offering annual TCD scans to children with SCD by 2011.

Follow up and failsafe arrangements

The SHT, in conjunction with local paediatric units, should have continuing responsibility for all children with SCD identified by the newborn screening programme, and should maintain a list.

100% of babies identified are to be registered by eight weeks by a designated healthcare professional at the paediatric unit of the local acute hospital. This local acute hospital must have links into an SHT to ensure that any major complications, together with an annual review, can be managed by appropriate multidisciplinary teams at the specialist centre.

All SHTs and LHTs should have robust follow-up arrangements to identify and follow up any child who does not attend their hospital appointments. They should also have the capability to track children who have moved out of the area in order to make appropriate handover arrangements.

Data Collection

(i) Anonymous data for 95% of children with SCD under the age of 5 should be submitted to the NHS Sickle Cell and Thalassaemia Screening Programme – please note that this data does not require consent.

i) 90% of children with SCD (whose parents have been offered information about the NHR and have given consent for the child's details to be included on the NHR) should have their details entered on to the Registry by end 2010.

* There was previously an additional standard, stating that 95% of infants should have completed the primary Prevenar (conjugate pneumococcal vaccination) course by 15 months. This was withdrawn because PCV13 is now given universally to all babies.

Recommendations and guidelines

These are based on current evidence-based practice and accepted good practice. Letter in brackets refers to the grading of the recommendation (see page 6).

Organisation of care

- There should be a network of care based on local community care (including GPs, the local sickle cell and thalassaemia centre - if available, health visitors and school nurses), the local hospital (LHT) and specialised centre (SHT) with links to paediatric intensive care where relevant. (C)
- Parents should be put in touch with local and national voluntary organisations and local sickle cell & thalassaemia centres. (C)
- There should be a named paediatrician responsible for follow-up in the local hospital. (C)
- There should be a named paediatrician and/or paediatric haematologist in the SHT. (C)
- General practitioners and community nurses should be kept informed on a regular basis. (C)
- Parents should be encouraged to acquire knowledge about their child's condition and should be informed about initiatives such as the Expert Patient Programme. (C)
- There should be community paediatric services to coordinate the community needs of the child and to liaise with CAMHS, local authority services and the voluntary sector as needed. (C)
- Local authority services (including education and social services) should be aware of the specific needs of children with SCD and their families. (C)
- CAMHS should be aware of the specific emotional and learning needs of children with SCD and their families. (C)

Identification of disease

All children born in England are offered screening for SCD as part of the newborn bloodspot screening programme. The Sickle Cell & Thalassaemia screening programme's aims and objectives are set out in Appendix 3.

Diagnosis is made by designated screening laboratories. Standards have been set for laboratories, as well as for the initial contact with the parent and registration in paediatric follow-up. (See Appendix 5).

Initial communication by the newborn screening programme

Bloodspots from newborn screening are sent to designated laboratories and the results of all infants with SCD are sent as a matter of urgency (e.g. by fax or email) to the nominated coordinating centre and named individual. The centre confirms receipt. Every area has a named healthcare professional which may be a paediatrician or a nurse. In some high prevalence areas the nurse will be a specialist in SCD. The parents of every affected child are informed by personal contact from the designated healthcare professional by 4-weeks after birth of the child.

Informing parents

Although women and their partners should have been offered antenatal screening and counselling and should have been fully informed of their risk, this may not always be the case in reality. It may still come as a shock to learn the diagnosis.[1] Early communication by the local named healthcare professional in a culturally sensitive way[2], is important to provide accurate information and to ensure that the infant has timely access to prophylactic treatment.

The primary care team needs to know the diagnosis as soon as possible to provide ongoing medical and emotional support and to begin penicillin treatment and immunisation with conjugate pneumococcal vaccination (see Outpatient care, page 17). Arrangements for outpatient follow-up should be made so that the infant is seen by 3 months of age.

Recommendations

- All parents/carers of an infant who has been diagnosed via the newborn screening programme should be given the result by the time the child has reached 4 weeks. This should be done in a culturally sensitive manner, respecting their dignity and individuality. An interpreter should be provided where necessary. (C)
- The result should be communicated to the family GP and health visitor as soon as it is received by the specialist nurse counsellor (SNC), or named healthcare professional. (C)
- Babies are to be registered by eight weeks by the designated healthcare professional within the LHT. This registration will include a request for diagnostic testing and confirmation that penicillin has been prescribed. (C)

- Appropriate written information about the condition should be provided for carers. (C)
- Parents should be given the opportunity to have genetic counselling, especially if they have not taken up this option before their child was born. (C)

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Confirmation of diagnosis

Newly diagnosed infants should be registered within the LHT by eight weeks of age by a designated healthcare professional so that the diagnosis can be confirmed and other family members can be offered screening tests if required.

Samples for diagnostic testing should be sent to a laboratory that is CPA-accredited and that takes part in quality control schemes for haemoglobin testing. There should be organised links with the neonatal screening laboratory to confirm cases identified by the newborn screening programme.

In the absence of the father's haemoglobin phenotype it may be difficult to get a definitive diagnosis, as HbSS, HbS/ß^0 Thalassaemia and HbS/HPFH all have an FS phenotype on screening. If there is any doubt, DNA analysis should be requested from a specialist unit.

Treatment should be instituted for all children until the diagnosis is clarified. There is no evidence that infants with HbS/HPFH need ongoing care and prophylactic treatment. However, this diagnosis should not be confused with a child with HbSS and a persisting high level of HbF, which is a relatively common finding.

Recommendations

- The diagnosis should be confirmed at the first sickle cell clinic visit by a laboratory accredited to carry out haemoglobinopathy testing. (C)
- Confirmatory results should be sent to the newborn screening laboratories for quality control. (C)
- DNA analysis should be requested in cases where the diagnosis is unclear. (C)
- Penicillin prophylaxis should be started while waiting for clarification of diagnosis, if this is delayed. (C)

Outpatient care

Organisation of follow-up

The majority of a child's care will take place at home, in an outpatient department or in a GP surgery. Many children require hospital admission at some time, but only a minority will require frequent admissions. As SCD is a lifelong condition it is important to engage the family early, not only to establish the diagnosis and start treatment, but also to provide advice, education and support.

The US Department of Health and Human Services' clinical practice guideline[1] outlines the importance of early entry into care for pneumococcal prophylaxis and the parents' ability to recognise and manage signs and symptoms of illness. In a Jamaican cohort study, parents were able to accurately define spleen size in cases of acute splenic sequestration; a potentially fatal complication if presentation is late.[2]

It is generally accepted that penicillin prophylaxis should start by 3 months of age, as the level of fetal haemoglobin starts to decline and the risk of splenic hypofunction increases. The Cooperative Study of Sickle Cell Disease, initiated in the USA in 1978, showed a significant number of acute events including bacterial meningitis and sepsis before the age of 6 months 3. Although there is no evidence for splenic hypofunction in HbSC and HbS/ß+ thalassaemia, the Cooperative Study showed a significant incidence of pneumococcal infections in HbSC in the first 2 years of life, indicating that these children should receive the same treatment and education as children with HbSS[3]. In order to achieve this, children should be registered for follow-up in the sickle cell clinic by 3 months of age.

The value of specific follow-up programmes for SCD, particularly after identification by neonatal screening, has been confirmed over the past 20 years. A US review of 10

years of newborn screening for SCD[4] described changing trends in survival, resulting not only from the introduction of penicillin, but also from the integration of children into routine follow-up and care. Improved survival has also been shown in a cohort study in Jamaica[5]. Enlistment in follow-up programmes following neonatal screening has been found to reduce morbidity and mortality to about 1%.[6] More recently, the benefit of regular TCD scans to identify those children at risk of cerebrovascular disease (see page 26) and to prevent stroke has been shown in a randomised controlled trial[7].

The aims of regular attendance in a local paediatric clinic with an LHT and annual review by a specialist sickle cell centre with an SHT should be to:

- Encourage adherence to treatment – particularly prophylaxis and immunisation programmes.
- Continue education.
- Offer screening tests.
- Monitor general health, nutrition and growth.

Treatment options can be offered depending on the nature of complications and transition to the adult clinic can be organised in a timely fashion. A policy for frequency of attendance at the specialist sickle cell clinic can be helpful, e.g. a minimum of 3-monthly during the first 2 years; 6-monthly until the age of 5 years; and annually thereafter.

Every child with SCD, regardless of where they live, should be offered annual access to a full range of specialist professionals (SHT) and services to ensure that their care is optimised. Some children may also need to be seen by the SHT before their annual review is due, in order to discuss particular management issues.

It is important that all families feel supported and have access to specialist advice and treatment. A qualitative study of pain management[7] showed that where families were supported and able to cope with their child's condition, the young adult was more likely to be able to manage their condition.

There should be regular communication with primary care and, where appropriate, the wider multidisciplinary team; and the parent-held book (provided to all newborns) should be completed on every visit. Arrangements for follow-up and shared care should be made explicit. A policy for tracking children who do not attend should be in place.

Recommendations

- The infant diagnosed through the newborn screening programme should be seen by the LHT or SHT by 3 months of age. (C)
- At the first visit the family should meet with a doctor and/or nurse experienced in the management of SCD who can give them accurate information and advice. (C)
- There should be regular communication between the SHT, the LHT, primary care and community nursing teams. (C)
- There should be a policy for monitoring attendance in clinic and for following up those families who fail to attend. This should include documentation of children who have moved to another area. (C)
- There should be ongoing support for the family and promotion of management of straightforward illness, including uncomplicated pain, at home. (C)
- There should be access to specialist assessment and treatment when required. (C)
- Every child should be reviewed at least once a year by the SHT; this may be by direct consultation, in an outreach clinic or within an MDT setting as appropriate. (C)

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The consultation

The following gives a guide to what should be included in each consultation. The list is not exclusive.

The history should include:

- Current symptoms and a review of painful episodes, illnesses, accident and emergency attendance and hospital admissions since the last consultation.
- A systematic enquiry about symptoms, e.g. abdominal pain, pica, priapism, headaches, snoring, other neurological symptoms suggestive of ischaemia.
- Adherence to penicillin prophylaxis.
- How pain and fever is managed at home.
- Regularity of school attendance and reasons for absence.
- Outcome of developmental screening tests, school progress and achievement in national tests (e.g. SATs, GCSEs).
- Travel plans.

The examination should include:

- Assessment of growth and development.
- A general physical examination that should take particular note of any pallor, jaundice, spleen size, presence of heart murmur.
- Blood pressure.

At the first consultation, investigations should include:

- Full blood count.
- Haemoglobin electrophoresis.
- Reticulocyte count.
- Blood group and extended red cell phenotype.

As G6PD deficiency is common in the same ethnic groups and also induces haemolysis. It is advisable to test for G6PD at the first newborn visit when the degree of reticulocytosis is unlikely to produce falsely elevated results.

Subsequent consultations: It is not necessary to take blood and urine tests at every visit. It is usually advised that steady state investigations (full blood count, renal and liver function tests) are carried out at 1 year of age to give a baseline. It is then possible to assess the severity of any subsequent acute problem.

Frequency of further investigations will depend on the clinical picture but routinely would not be performed more than once a year.

The reason for blood and urine tests and other screening tests in well children is to provide a baseline should the child become unwell, and to screen for conditions that may benefit from treatment. Blood tests should generally be performed annually unless there is clinical concern. Steady-state oxygen saturations should be recorded.

TCD scans should be carried out annually from age 2 years (or earlier at the discretion of the clinic).

Prevention of infection

A major aim of neonatal screening and follow-up care is to reduce the morbidity and mortality from preventable disease by antibiotic prophylaxis and immunisations.

Splenic hypofunction resulting from splenic infarction, usually from the first 6 months of life, means that children are at a greatly increased risk of infection by organisms expressing polysaccharide antigen, such as pneumococcus and Haemophilus influenzae.

Children with SCD are more likely than the general population to be transfused for complications such as acute splenic sequestration or aplastic crisis; some 5-10% may be enrolled on a chronic transfusion programme at some time in their life.

Protection against hepatitis B should be arranged before exposure is likely to occur.

Many families travel to parts of the world where malaria and meningococcus are endemic, and they should receive appropriate advice and prophylaxis. Malaria is likely to be a serious issue due to splenic hypofunction. Families should be aware that having SCD does not make a person immune to malaria.

Adherence may be a problem: Published reports show about 70% compliance with treatment. Failure to administer penicillin may be due to parental health beliefs[1] and practicalities of renewing prescriptions.[2] A synthesis of qualitative studies[3] shows a widespread resistance in general to taking medication for any condition over prolonged periods.

Penicillin prophylaxis

In a randomised controlled trial it was shown that penicillin was effective in reducing the mortality from pneumococcal sepsis[4]. Published guidelines recommend that penicillin prophylaxis is lifelong[5]. As compliance is likely to decline and the incidence of pneumococcal infection in the community reduces significantly after the age of 5 years[6], the emphasis should be on excellent adherence in early childhood.

Penicillin V should be offered to all children according to the following dosage schedule:

- 62.5mg po bd <1yr
- 125mg po bd 1-5yr
- 250mg po bd >5yr

Erythromycin is a suitable alternative if penicillin allergy is documented.

Vaccine	Age
DTaP/Hib/IPV + PCV13	2 months
DTaP/Hib/IPV polio + Men C	3 months
DTaP/Hib/IPV + Men C + PCV13	4 months
Hep B + Hib/Men C	12 months
MMR + PCV13 + Hep B	13 months
Hep B	18 months
Pneumovax	2 years
Pneumovax	7 years
Pneumovax	12 years
Pneumovax	17 years
Influenza	Annually from 6 months

DTaP/Hib/IPV is a single vaccine that protects against diphtheria, tetanus, pertussis, Haemophilus influenzae and polio.

PCV13 is a conjugate vaccine that protects against 13 serotypes of pneumococcus.

Hib/MenC is a combined vaccine that protects against Haemophilus influenza and meningitis C.

If PCV13 is not given during the first year, two doses should be given 2 months apart in the second year.

Pneumovax (23 valent polysaccharide pneumococcal vaccine) should be given in addition at 2 years (and 5-yearly thereafter) at least 2 months after PCV13.

Travel requirements

Meningitis ACWY is recommended for travel to sub-Saharan Africa and Saudi Arabia in addition to other recommended travel vaccinations and malaria prophylaxis.

Recommendations

- Twice-daily penicillin prophylaxis or alternative should be prescribed by 3 months of age and continued throughout childhood. (A)
- Local negotiation should be carried out between hospital, GPs and pharmacies to ensure a reasonable length of prescription to encourage compliance. (C)
- Reasons for parents not giving their children penicillin should be explored and addressed as fully as possible. (C)
- Immunisation against pneumococcal infection should include PCV13 and Pneumovax according to national schedules. (C)
- A course of hepatitis B immunisation should be offered to the non-immune child. (C)
- Annual influenza immunisation should be offered. (C)
- If appropriate, malaria prophylaxis should be strongly recommended and current guidance sought for the area of travel. (C)

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Education about SCD

The following topics should be emphasised at every clinic visit or contact with the team. The aim is to educate parents (and then the children themselves) to manage uncomplicated problems at home. In addition, they should be taught to recognise the onset of serious complications so that the child is brought promptly for hospital treatment. Where possible, this information should be backed up by written material in the first language of the parents with interpreters available as required. The following list is not exclusive:

- A simple understanding of the condition.
- Importance of penicillin.
- Importance of staying up-to-date with all vaccinations.
- Management of pain at home.
- Need to seek early advice for fevers, respiratory symptoms or other signs of infection, priapism and how to access advice and admission if necessary.
- Recognition of unusual pallor and need to seek early treatment.
- Need to seek early medical advice if weakness (without pain), tingling, loss of speech, or any neurological complications are observed.
- Detection of an enlarged spleen by palpation.
- Recognition of dactylitis and other painful crises.
- Symptoms and signs of priapism
- When to consult the GP.
- When to come to hospital in an emergency.
- Need for reporting any visual symptoms.
- Need to report any developmental concerns or falling-off in school achievement.
- General advice regarding keeping warm and avoiding sudden changes in temperature, care when swimming, maintaining a good fluid intake
- Information that should be shared with the child's school.
- The need for any planned surgery to be managed jointly with the surgeon, anaesthetist and the SCD (LHT and/or SHT) team.
- Travel advice.
- Genetic counselling, contraception.
- Avoidance of smoking and alcohol.

Recommendations

- Every outpatient visit should provide an opportunity for ongoing education of the child and family. (C)
- There should be a systematic approach to education which will vary at different ages. (C)

The annual review

This should include assessment of progress in general and a review of the patient's and family's knowledge of the condition by an experienced doctor, usually the SHT which will include consultant and a clinical nurse specialist or nurse counsellor. If possible, a clinical psychologist should be available at the same visit. The annual review can take place at either the SHT site or LHT site depending on local circumstances. There should be a written policy on annual review devised by the SHT.

- Review of information provided by the LHT at the local hospital – to include any investigations taken, treatment given.
- Clinical review:
  - Number of hospital admissions.
  - Number and severity of crises (include days off school).
  - Other complications e.g. splenic sequestration, aplastic crisis, priapism, gallstones, chest syndrome, stroke.
  - Nocturnal enuresis >6 years.
  - Assessment of child development.

- Review of infection prevention:
  - Penicillin V dosage and compliance.
  - Immunisation record.
- Clinical measurements – undertaken at visit or results of investigations since last visit reviewed:
  - Clinical examination – heart, lungs, liver, spleen.
  - Assessment of growth and development
  - Blood pressure.
  - Oxygen saturation.
  - Urinalysis.
- Consideration and discussion of other treatments, e.g. hydroxyurea, bone marrow transplantation.
- The annual review also provides an opportunity for collection of data as required by the NHS Sickle Cell and Thalassaemia Screening Programme and the National Haemoglobinopathy Registry (refer to Appendix 7 and Appendix 8 respectively)

Transition to adult service

Transition is 'the purposeful planned movement of adolescents and young adults with chronic physical and medical conditions from child-centred to adult-oriented health care systems.'[1]

The importance of transitional care has been highlighted in the Children's National Service Framework Hospital Standards[2], *Improving the transition of young children with long term conditions to adult health services*[3] and the intercollegiate report, Bridging the gaps: health care for adolescents[4]. This includes a requirement for children and adult services to take the needs of this group of patients into consideration when planning and developing services.

The 2004 National Service Framework for Children[5] emphasises the importance of transition and states that within 10 years, ideally: 'Transition to adult services for young people is planned and coordinated around the needs of each young person to maximise health outcomes, their life chance opportunities and their ability to live independently.'

There is a need to involve the GP and community services early in the process, as they may be expected to take on a wider role as children leave the holistic care of paediatric outpatients

In paediatric care, services place very few medical management expectations on the adolescent (these being placed instead on their parents) and clinicians are generally knowledgeable about the patient's condition. In contrast, adult healthcare services may know less about patients and/or how their condition affects them, but generally have higher expectations for medical self-management. In addition, adolescents, by definition, have to cope with numerous changes as they develop their individual identity and deal with personal priorities of school, work, friends, family, social relationships and independent living.

Perhaps the biggest fear for adolescents is how their painful episodes are going to be managed in hospital on an adult ward. There may be significantly lower supervision and direct nursing care on the adult ward and a reasonable expectation that the adolescent will take a more active role in managing painful episodes. There may be fewer visits from doctors and less structured activity, including school-work supervision. In addition the medical staff will initially be unfamiliar with the individual and the 'adult' analgesic regimen may differ from the paediatric one.

Research indicates that adolescents with SCD have concerns, opinions and expectations about their future healthcare and medical management. They need guidance, support and information about available services to help meet daily challenges.[6] Adolescents with SCD may have problems of adjustment during a transition phase[7]; and it is important to identify factors that would guide appropriate interventions.

Arrangements need to be flexible, as children reach maturity at different ages and puberty in general is delayed. Hospital policy may demand that all children are admitted to adult wards at the age of 16 years, even when they are emotionally and sexually immature. The following recommendations are based on experience from existing transition clinics in sickle cell centres.

Recommendations

- There should be a hospital transition policy in place and preparation and planning should start at an early age, e.g. at age 13-14 years. (C)
- A detailed review should be carried out at 15-16 years to include knowledge and understanding about SCD, management, concerns about healthcare in an adult setting and readiness to transfer. (C)
- A transition or adolescent clinic should be available to allow the adolescent to meet the adult sickle cell team and for a formal review and handover to take place. (C)

- Adult and paediatric protocols for managing complications, in particular painful episodes, should correspond as much as possible. (C)

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Ongoing issues and chronic complications

Management of pain at home

Quite commonly, children experience pain at home. This is usually mild to moderate and it will not be necessary to bring the child to hospital. Frequent pain may lead to other problems, including negative mood, and considerable loss of schooling.

It is important for older children, parents/carers and family members to know how to manage pain at home with appropriate analgesia for the level of intensity. In addition, coping strategies have to be examined since these have been shown to predict both pain experience and the utilisation of health services.[1]

Paracetamol and ibuprofen are the analgesics of choice in mild-to-moderate pain. Codeine phosphate can be added for more severe pain, but it should be recognised that at least 20% of cases will not respond due to the lack of the enzyme needed to convert it to morphine.[2] If there is no response to these, the child should be assessed in hospital.

An individual care plan should be available for all children in the A&E department (or children's ward if there is a direct admissions policy). It is usual to advise an increase in fluid intake if the child is unwell, as dehydration will tend to prolong the painful episode.

Recommendations

- Parents/carers and older children should be given clear guidance on how to assess and manage pain at home, including the type and dose of analgesia to be used for different levels of pain intensity, and when to seek medical advice. (C)
- Parents/carers should be informed about non-pharmacological therapies for pain, such as massage. Children should be encouraged to use psychological coping strategies, including distraction techniques such as games, computers and television. (C)
- Children should be encouraged to identify and avoid factors that regularly trigger acute pain, such as exposure to cold weather, excessive physical activity and dehydration. This information should also be passed on to the school by a competent healthcare professional. (C)

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Nutrition and growth

Impaired growth, poor nutritional status and delayed skeletal and sexual maturation are common in children with SCD.

In HbSS, growth retardation may become apparent after 6 months of age – possibly due to decreased absorption of nutrients and/or an increase in the metabolic rate. Poor appetite is frequently reported, and anorexia associated with febrile or painful episodes is common.

Studies of body composition show a significantly lower fat mass in prepubertal children and lower fat-free mass in all children, with muscle wasting and low protein stores.[1]

There is some evidence that growth can be accelerated by providing extra calories via naso-gastric feeding.[2]

There is little evidence of specific nutrient deficits, although a randomised control trial[3] showed some improvement in height and weight after supplementation with zinc sulphate. Another controlled trial[4] showed a reduction in infections and hospital admissions in those taking zinc supplements.

As a hypochromic microcytic blood picture may be caused by an associated thalassaemia trait, iron supplementation should be given only if iron deficiency is documented. There is no evidence that folic acid supplementation is beneficial, although many parents choose for their children to take it[5,6].

Vitamin D deficiency is very prevalent in non-white children of all ages in the UK[7, 8] and there has been a resurgence of rickets. Advice should be given regarding vitamin supplementation, an adequate calcium intake and exposure to sunlight. The Consensus Development for the Supplementation of Vitamin D in Childhood and Adolescence[9] recommends 400 IU vitamin D daily in the first year of life, regardless of manner of feeding, and 200 IU to the age of 50 years.

Some clinicians recommend the use of ethnically appropriate growth charts[10], but not specific sickle cell charts. Puberty may be delayed by about 6 months in Hb SC and by 2-3 years in HbSS.[11] Delayed skeletal maturation during adolescence allows for a longer growth period in the long bones. This results in normal adult height, and hence children and their parents can usually be reassured. Hormonal treatment may be indicated in children with physiological delay if they are very concerned by their short stature.

An endocrinology opinion should be sought if there are no physical signs of puberty in a girl at 14 years and a boy at 14.5 years.[12] It should also be recognised that children on long-term transfusion programmes with significant iron overload may develop pituitary +/- primary gonadal deficiencies.

Recommendations

- Heights and weights should be measured at each visit and plotted on appropriate growth centile charts. (C)
- Referral to a dietitian should be made to consider extra caloric input if the child is hospitalised for frequent or long periods. (C)
- Zinc supplementation should be considered if growth is retarded. (B)
- Vitamin D deficiency should be treated. (C)
- Children with delayed growth should be reassured if there is evidence of delayed skeletal maturation. However, they should be referred to a paediatric endocrinologist if there are no physical signs of puberty at 14 years in a girl and 14.5 years in a boy. (C)

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Nocturnal enuresis

Nocturnal enuresis is common in all children, and approximately 15% of children aged 5 years and 3% of 15 year olds still wet the bed.

There is an increased rate of nocturnal enuresis in SCD, particularly in boys with HbSS; but, as in the normal population, most will resolve spontaneously. The reason for this is not entirely clear. Children pass large quantities of dilute urine and have nocturia, but this should not necessarily lead to incontinence. Overnight urinary volumes greater than maximum functional bladder capacity have been posed as a possible cause.[1]

Parents report that their children are heavy sleepers. It has been shown that children with adenoidal hypertrophy and obstructive apnoea are more likely to have nocturnal enuresis[2] and it is possible that hypoxaemia plays a role in the aetiology of nocturnal enuresis.

On the whole, sickle cell children do not respond to behavioural management techniques such as star charts or mattress alarms but can be 'trained' by intermittent alarms and parental waking to achieve continence. Many children respond to oral or nasal desmopressin, and this is a useful adjunct, particularly for school trips.

Recommendations

- If nocturnal enuresis is present over the age of 6 years, this should be documented and parents should be given information and advice on treatment. (C)
- If the history is suggestive of obstructive apnoea and snoring, this should be documented, overnight oxygen saturations should be measured and a referral made for an ENT opinion. (C)
- Desmopressin therapy should be considered in those children who do not respond to routine advice and management. (C)
- The child should be referred for specialist management (e.g. an enuresis clinic) if there is no response to basic measures after the age of 7 years. (C)

References

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Liver disease

Gallstones occur in over 50% of children with SCD over the age of 10 years in the UK[1]. They are usually asymptomatic and may not be the cause of intermittent abdominal pain, which is relatively common. There is no evidence to recommend cholecystectomy in asymptomatic cases, but it is advised in symptomatic biliary disease.

Recommendations

- Annual steady-state liver function tests should be carried out. (C)
- Recurrent episodes of abdominal pain should be investigated with an ultrasound of liver and biliary tree. (C)
- Elective cholecystectomy should be carried out in symptomatic biliary disease. (C)

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Avascular necrosis of the femoral and humeral head

This may occur in all genotypes and children with high HbF levels are not protected. The shoulder joint is more likely to be affected in older age groups. Although weight-bearing makes femoral head necrosis more likely to cause severe joint destruction, healing with minimal destruction may be the outcome if it occurs before closure of the femoral epiphysis.

X-ray changes will not be apparent until the repair process has changed the density of the bone. Hence MRI scanning is the investigation of choice in a persistent painful hip or shoulder.

It is usual to use some form of radiological staging to evaluate the development and progression of the disease.[1]

Initial treatment should be conservative, with analgesia, partial weight-bearing on crutches and physiotherapy support.

Recommendations

- An MRI scan should be carried out where there is persistent pain in the hip or shoulder. (C)
- The radiological stage of avascular necrosis should be documented. (C)
- Referral to an orthopaedic surgeon with an interest in SCD should be undertaken if pain persists or if avascular necrosis is at stage III or more. (C)

References

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Leg ulcers

These are relatively uncommon in children in the UK. Nearly all ulcers develop in the ankle region near the malleolus and often exist bilaterally. They may be painless or extremely painful. The pathogenesis of this condition is uncertain, but is likely to result from poor microvascular bloodflow of abnormal red cells combined with reduced oxygen delivery. Low serum zinc levels have been reported in non-sickle patients with venous leg ulcers. However, low serum zinc levels are found in all patients with SCD and do not correlate specifically with leg ulcers. A controlled study of a small number of patients taking oral zinc sulphate did, however, accelerate healing of leg ulcers.[1]

There has been a randomised double blind controlled trial using granulocyte-macrophage colony stimulating factor (GM-CSF) in non-sickle patients with chronic venous leg ulcers with acceleration of healing.[2] Another study showed good response using topical GM-CSF in a small number of sickle patients.[3] Best practice is not clear in this group and neither regular transfusion therapy nor hydroxyurea therapy seems to influence outcome.

In the first instance ulcers should be treated with frequent dressing, support bandages and antibiotics if infected. Physiotherapy to increase ankle mobility and venous return is also likely to be helpful.

Recommendations

- Debridement of the ulcer and antibiotic therapy should be started if infection is present. (C)
- Adequate pain relief should be prescribed. (C)
- Compression bandaging and physiotherapy should be arranged to improve ankle mobility. (C)
- Oral zinc sulphate should be considered in children with persistent leg ulcers. (B)

References

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Cerebrovascular disease

In a multicentre sickle cell cooperative study in the USA, the overall incidence of stroke in SCD (HbSS) was 0.6/100 patient years. The highest incidence was between 2 and 5 years (1.02/100 patient years) and by the age of 20, about 11% of people with SCD had a clinically evident stroke[1]. In the absence of primary screening and prophylaxis, there is no reason to expect rates to differ in the UK.

In children, the cerebral ischaemic damage is often in the territory of supply of the internal carotid/middle cerebral artery. However, damage in a watershed distribution between the anterior and middle cerebral artery, or middle and posterior cerebral artery, are also commonly observed.

Stroke is associated with cerebrovascular stenotic lesions, commonly in the distal internal carotid and proximal portions of the middle cerebral and anterior cerebral arteries. The high bloodflow velocities through these stenotic segments can be detected using TCD ultrasound scanning.

A large prospective follow-up study showed that a high-risk group for stroke can be identified by time-averaged mean velocities in the ICA/MCA/ACA segments >200cm/sec. The risk is also increased to a lesser extent in those with conditional velocities (170-200cm/sec) and in those with absent or low signal. This randomised, controlled trial showed that a first stroke could be prevented by regular

blood transfusions in children with SCD and abnormal TCD scans[2].

The recent UK guidelines for diagnosis and management of stroke in childhood[3] has incorporated the conclusions from this and other studies and recommends annual screening for stroke in children with SCD from the age of 2 years (or earlier at clinical discretion).

Another important indicator of risk for stroke is a history of transient ischaemic attacks. Other reported risk factors – such as low baseline haemoglobin, high baseline leukocyte count, low overnight oxygen saturation,[4] acute chest syndrome in the previous 2 weeks, frequent episodes of acute chest syndrome and high systolic blood pressure[5] – are too insensitive to be of any value in evaluating a child, although high blood pressure obviously requires appropriate investigation and management.

Stroke is more prevalent in HbSS and HbS/ β^0 thalassaemia compared to HbSC and HbS/ß+thalassaemia, although there is limited information regarding HbS/β^0 thalassaemia.

Haemorrhagic stroke is relatively rare in childhood, becoming more common in the third decade. Identified risk factors include low haemoglobin and high white cell count. Intracerebral aneurysms are more common in SCD and can be multiple. The pathogenesis is unclear. There are no established or proven ways of screening for increased risk of haemorrhagic stroke.

About 17% of children with sickle cell anaemia have silent infarcts on MRI scan that are not associated with overt neurological episodes or symptoms. These are relatively small white-matter lesions, often in the anterior watershed distribution. They are associated with mild cognitive impairment, which may be picked up by neurocognitive screening tests.[6] TCD screening in these patients shows normal results in 75% of cases; and there is, as yet, no evidence that silent infarcts can be prevented by blood transfusion or other intervention.

The relative hazard for overt stroke in a patient with a silent infarct is approximately 14 times those with a normal MRI. This compares to 18 times normal in a patient with a high-risk TCD.[7]

Chronic transfusion has been established as effective secondary stroke prevention, reducing the risk of recurrent stroke from 50-75% to about 13%[8]. The aim of the transfusion regimen is to maintain haemoglobin S below 30%. Some patients may be able to reduce the intensity of transfusions after 3 years to maintain haemoglobin S at 50%.

The second stroke prevention trial in sickle cell anaemia in the USA[9] recommends that transfusion therapy should be continued throughout childhood. This is because a significant number of children reverted to the high-risk range of TCD velocities or developed overt stroke after discontinuation.

As iron overload is a serious consideration in long-term transfusion therapy, clinical decisions will need to be reached on a case-by-case basis.

Recommendations

- Annual TCD scans should be performed on all children with SCD from aged 2 years in accordance with the TCD Standards and Guidelines attached in Appendix 10. For those children who are considered to be "high risk", the risks and benefits of starting regular blood transfusions and/or other treatments should be fully discussed by an appropriate multidisciplinary team with parents/carers (A)
- The symptoms and signs of stroke should be discussed with parents/carers in the first two years of life and information given on what action to take should the child develop neurological symptoms. (C)
- Appropriate imaging studies to assess the extent of cerebrovascular disease should also be arranged if there is evidence of cerebral vessel narrowing on TCD, learning difficulties, atypical symptoms such as unusual behaviour during acute pain, frequent headaches, fits or other unexplained neurological, psychiatric or psychological symptoms. (C)
- Blood pressure should be measured and recorded annually. (C)
- Overnight oxygen saturation monitoring should be recorded if there is a history of snoring, nocturnal enuresis after the age of 6 and low steady-state oxygen saturations on air (<95%). (C)
- Children should have access to a neuropsychologist to assess cognitive function, learning and behavioural difficulties. (C)
- Transfusion therapy should be offered throughout childhood for the secondary prevention of stroke. (B)

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Kidney disease

Renal complications are relatively common in SCD, particularly with increasing age.

Renal failure primarily due to SCD is rare in childhood, but other paediatric complications include urinary tract infections, haematuria, microscopic albuminuria and renal papillary necrosis. There is little good information on the frequency of these problems in childhood or whether screening for renal disease in childhood, such as by microcopic albuminuria, leads to intervention that can prevent problems in later life.

Recommendations

- Any child with a urinary tract infection should be treated and then investigated according to Royal College of Paediatrics and Child Health guidelines. (C)
- Macroscopic haematuria should be fully investigated according to local protocols. (C)
- Blood pressure, urea, creatinine and electrolytes should be measured on a yearly basis and renal investigations initiated if hypertension is present or if there are raised creatinine and urea levels. (C)

References

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Lung disease

Acute chest syndrome is a well-characterised complication of SCD in childhood.[1] It is a potentially fatal complication, and there is good evidence that recurrent episodes can be prevented by hydroxyurea.[2]

Chronic lung complications are increasingly recognised, particularly in adults. Two main chronic problems are recognised: Chronic sickle lung, with a restrictive lung picture; and pulmonary hypertension. Both are predominantly a problem in adulthood, but with increasing recognition in older children and adolescents.

Anecdotal evidence suggests that in chronic sickle lung, deterioration can be prevented by hydroxyurea or regular blood transfusions. It is therefore potentially important to detect early development of these problems in children.

Low blood-oxygen saturations, as assessed by overnight oxygen by pulse oximetry, have been linked to both cerebrovascular disease and frequent episodes of acute pain. Referral to a respiratory physician with an interest in SCD should be made if there is evidence of pulmonary hypertension[3].

Recommendations

- Children with either two or more episodes of acute chest syndrome in the last 2 years, or one episode requiring ventilatory support, should be offered hydroxyurea. (A)
- Oxygen saturations in air should be recorded on an annual basis using pulse oximetry when the patient is well and seen in outpatients. If saturations are <95%, overnight oxygen saturation monitoring should be performed. (C)
- If the mean overnight oxygen saturation is <95%, the child should be investigated for cerebrovascular disease and obstructive sleep apnoea (see management of acute neurological complications, page 51). Formal pulmonary function tests and echocardiography should also be arranged. (C)
- If pulmonary function tests suggest chronic sickle lung, the child should be monitored with regular pulmonary function tests. Overnight pulse oximetry and high-

resolution CT scan of the lungs should be considered. Treatment with home oxygen, hydroxyurea or regular blood transfusions should be considered in cases of deterioration. (C)

- Echocardiography to assess pulmonary hypertension should be arranged if there is evidence of chronic sickle lung, chronic unexplained hypoxia (oxygen saturations <95%) or other symptoms/signs suggestive of pulmonary hypertension. (C)
- A child with significant pulmonary hypertension should be referred to a respiratory physician with an interest in SCD. (C)

References

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Priapism

(see also management of fulminant priapism, page 39)

Priapism mainly affects adolescents and adults, and may go unreported.

Bicorporal priapism occurs in 3-5% of pre-pubertal boys and has a better prognosis for normal erectile function than tricorporal priapism in post-pubertal boys. Events may be classified as stuttering (occurring for less than 3 hours' duration but several times a week), minor (isolated orinfrequent episodes of less than 3 hours' duration), or major (events usually lasting more than 3 hours – see section on acute management).

Major episodes are often preceded by bouts of stuttering priapism. In minor episodes bladder emptying, exercise such as jogging, warm baths and analgesia may help abort an attack. Oral etilefrine may reduce the frequency of stuttering priapism[1] and, in a prolonged episode, aspiration and irrigation of the corpora cavernosa with epinephrine or etilefrine is now the treatment of choice.[2]

Children and their carers should be advised to seek treatment early and should attend hospital as an emergency if priapism persists for more than 2 hours.

Recommendations

- All boys and their parents/carers should be warned early in childhood about priapism being a complication of SCD. (C)
- Adolescent boys and their parents/carers should receive further information about priapism and know to seek treatment early. (C)
- An enquiry about priapism should be included as part of the outpatient consultation for pubertal boys. (C)
- For minor events, complete bladder emptying before sleep, pain relief and warm baths should be recommended. (C)
- Oral etilefrine should be considered in cases of stuttering priapism. (C)

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Eye complications

Sickle cell vaso-occlusive events can affect every vascular bed in the eye and may have serious and permanent visual consequences. Detectable retinal disease is very rare in childhood, being found most commonly between the ages of 15 and 30 years. Patients with HbSC and HbS/ß thalassaemia are more likely than those with HbSS to have serious ocular problems[1].

The clinical manifestations are grouped according to whether there is neovascularisation or not. In non-neovascular or 'non-proliferative' cases, there are rarely any visual consequences. In contrast, revascularisation and proliferation may proceed to vitreous haemorrhage and retinal detachment. However, there is a high rate of spontaneous regression or non-progression and indications for treatment are not clear.[2]

Given the uncertainty about the natural history of this complication, there is no evidence to support routine ophthalmologic screening of children. Children and their carers should report any change in vision and be referred for an ophthalmologic opinion as a matter of urgency.

Recommendations

- Children and their carers should be made aware of this potential complication. (C)
- Any visual symptoms should be reported immediately and the child referred urgently for an ophthalmologic opinion. (C)

References

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Routine surgery and peri-operative care

As well as needing operative procedures for sickle cell complications such as acute splenic sequestration or gallstones, children may need routine operations for adenoidal hypertrophy, serous otitis media, orchidopexy, dental extractions and other complications that occur in childhood. There is no consensus among anaesthetists and haematologists as to which children need pre-operative transfusion, and some units are very much more conservative in their approach than others.

Peri-operative management plan

All patients with SCD, even if not previously severe, are at increased risk of sickle complications at time of surgery. Certain patients are at greater risk of peri-operative complications:

- Those with severe sickle-related problems such as acute chest syndrome, cerebrovascular disease and frequent painful episodes.
- Those with severe obstructive sleep apnoea.

The peri-operative management of patients with SCD requires good communication between surgeons, anaesthetists, haematologists, paediatricians and nursing staff. A clear management plan should be written in the notes prior to surgery.

Pre-operative transfusion

The optimal pre-operative transfusion policy in SCD is not clear. There is only one randomised controlled trial[1], which showed that a conservative transfusion regimen which raised haemoglobin to 10g/dl was as effective in preventing peri-operative complications as an aggressive exchange regimen which reduced HbS to <30%.

Major surgery (including cardiovascular surgery and neurosurgery) typically requires transfusion.

The situation is less clear for moderate and lower risk surgery such as cholecystectomy[2] and adenotonsillectomy.[3,4]

A randomised trial is currently being run by the National Blood Service in conjunction with the MRC Clinical Studies Unit [5]. This compares those who receive no transfusion with those who receive additive or exchange transfusion.

Recommendations

- A clear management plan, agreed by all healthcare professionals involved, should be written in the patients' notes before surgery. (C)
- SHT should have guidelines on pre-operative transfusion in patients with SCD to share with LHTs. (C)
- The transfusion lab should have a red cell phenotype and recent antibody screen performed in case blood transfusion becomes necessary before or after the operation. (C)
- SHT should have guidelines on the procedure for surgery to share with LHTs, including the use of fluids, oxygen therapy and antibiotics and postoperative care. (C)

References

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Specific treatments

Hydroxyurea

(hydroxycarbamide)

Hydroxyurea promotes fetal haemoglobin synthesis, improves red cell hydration, decreases neutrophil count, modifies red cell-endothelial cell interactions and acts as a nitric oxide donor.

There have been two randomised controlled trials looking at efficacy of hydroxyurea in SCD. The Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) [1] showed a reduction in frequency of painful episodes, incidence of chest syndrome and transfusion requirement without serious short-term side effects. A paediatric study in Belgium[2] showed similar beneficial results. Long-term data from the MSH study has shown a reduction in mortality in the hydroxyurea group.

There are a number of side effects, of which myelosuppression is the most common in the short term. In conditions already predisposed to leukaemia (e.g. polycythaemia rubra vera) there is an increase in the incidence of leukaemia in patients who received hydroxyurea treatment. There is no evidence to date from its use in SCD to suggest that children on hydroxyurea are more at risk.

Long term teratogenic risk is also not known, but sexually active individuals taking hydroxyurea should be advised to use contraception.

Hydroxyurea is of benefit to both children and adults with moderate to severe SCD.

There are still some areas which need clarification: The optimal dose; impact on long-term organ function and risk of malignancy. For these reasons, its use should be monitored with collection of data about long-term outcomes.

Recommendations

- Hydroxyurea should be considered in patients who have recurrent episodes of acute pain (more than three admissions in the previous 12 months, or are symptomatic in the community) or who have had two or more episodes of acute sickle chest syndrome. (A)
- The decision to start hydroxyurea should be made by the SHT, although the LHT will have a role in monitoring blood counts and side effects. The SHT should have a written protocol which is shared with the LHTs. This should include information about dose regimen, frequency of blood test monitoring, management of myelosuppression and contraindications for use of hydroxyurea. (C)
- The patient and/or their parents/carers should be given a patients' information sheet and the use of hydroxyurea should be discussed with them on at least two separate occasions. Current knowledge about side effects, including subfertility, cytopenias and the possible risk of leukaemia or other malignancies should be discussed. This discussion should be documented in the patient's notes. (C)

References

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Use of transfusion therapy

(see also sections on lung disease, cerebrovascular disease and peri-operative management)

Transfusion is an essential and life-saving therapy for some acute complications of SCD and has been shown to reduce the risk of chronic progressive organ damage in the case of ischaemic stroke.[1,2] There may be a beneficial effect in preventing other forms of organ damage, but studies are currently lacking.

Transfusion should not be undertaken without careful consideration of the benefits and risks. Informed consent from the parents, or child where appropriate, should always be obtained prior to transfusion.

There is an incidence of about 18% of alloimmunisation following blood transfusion in the sickle population, and two thirds of antibodies described are in the Rh or Kell systems.[1] This is in part because the blood donor population and sickle-patient population are from different ethnic origins. [2] The risk of alloimmunisation can be reduced by transfusing only if absolutely necessary and using blood that is fully Rh and Kell typed.

There is an incidence of delayed haemolytic transfusion reactions in SCD of between 4% and 22%, which is significantly higher than in other patients.[3] These can mimic sickle cell crises, and the clinician should have a high

index of suspicion for investigating for the development of antibodies when crises develop in the post-transfusion period.

Once an alloantibody has been identified, antigen-negative blood should be given. Hyperhaemolysis has also been described post transfusion without the development of antibodies. This may be due to bystander haemolysis and one study has shown a benefit of high-dose steroids and intravenous immunoglobulin.[4]

Viscosity of blood-containing sickled cells increases with increasing haemoglobin, so it is important to balance target haemoglobin levels with haemoglobin S concentrations. With this in mind, the target of a top-up transfusion for the treatment of acute anaemia is to the steady-state haemoglobin level. In monthly top-up transfusions (e.g. for the management of stroke where the haemoglobin S is being maintained <30%), the target haemoglobin is between 12 and 13g/dl.

Urgent blood transfusion may be beneficial in some acute complications. The aim is usually to correct the anaemia and sometimes to reduce the haemoglobin S level below 30% or 50%. Reducing the HbS level below 30% will often require an exchange transfusion, although a top-transfusion may be adequate if the child is initially very anaemic. As children with SCD may be candidates for bone marrow transplantation, CMV negative blood should be used in all CMV negative children.

Indications for acute transfusion

- Acute anaemia
  - o Parvovirus B19 infection
  - o Acute splenic or hepatic sequestration
- Acute chest syndrome – early top-up transfusion may avoid the need for exchange transfusion
- Stroke or acute neurological deficit – exchange transfusion is usually necessary to reduce the HbS to less than 30%, Hb10-11g/dl.
- Multiorgan failure
- Preparation for urgent surgery

Indications for regular, long-term transfusion

- Primary and secondary stroke prevention
- Recurrent acute chest syndrome not prevented by hydroxyurea
- Progressive organ failure

Recommendations

- At diagnosis or first clinic attendance, all patients should have an extended red cell phenotype performed. (C)
- All blood transfused should be fully Rh and Kell compatible. If alloantibodies are identified, further transfusions should be negative for corresponding antigen. CMV-negative blood should be used in all CMV-negative children. (C)
- Red cells for transfusion to patients with SCD should be sickle test negative and less than 7 days old if possible. (C)
- Urgent red cell transfusion should be used in children with rapidly progressive acute chest syndrome and acute neurological symptoms aiming to achieve HbS level below 30% and Hb 10-11g/dl. This will often require an exchange transfusion. (C)
- Long-term transfusion regimens should be used after a cerebrovascular event to prevent recurrence and considered if cerebral vessel velocities are classified as "high risk" on TCD scans as set out in the TCD Scanning Standards & Guidelines attached in Appendix 10. (A)
- Iron chelation should be started in all children on regular blood transfusions according to standard protocols. (C)
- Immunisation against hepatitis A and B should be offered to all those on long term transfusion programmes. (C)
- Children receiving regular monthly blood transfusion should have a specific annual review. (C)

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Bone marrow or stem cell transplantation

Bone marrow/stem-cell transplantation is the only treatment for SCD which is potentially curative.

Published experience describes a 92-94% survival rate and a 75-84% disease-free survival rate.[1-3] There is no recurrence of clinical vaso-occlusive events in patients with stable engraftment, but 10% of patients experience rejection or recurrent SCD. The majority of patients have an excellent quality of life after bone marrow transplantation (BMT).

There are, however, significant risks associated with BMT. The most common early complications are acute graft-versus-host disease (GVHD) and neurological events, including intracerebral haemorrhage and seizures. Chronic GVHD is the most common cause of late mortality and morbidity, with an incidence of 5% in the UK. Other late complications include gonadal dysfunction and an increased risk of malignancy.

Unlike thalassaemia major, where the clinical course is fairly predictable, there is a large variation of severity in SCD. In view of this, and the high risk of mortality and morbidity from the procedure, BMT is not appropriate in every patient. The British Paediatric Haematology Forum suggested criteria for selection[4, 5]

Acceptance

- <17 years with HLA-identical sibling and informed consent
- One or more of these SCD-related complications:
  - CNS disease
  - Recurrent acute chest syndrome
  - Stage I/II chronic sickle lung disease
  - Recurrent, severe, debilitating pain (>3 hospital admissions/year in 3-4 years)
- Problems relating to future care – to be decided on case-by-case basis

Exclusions

- Donor with a major haemoglobinopathy
- One or more of the following:
  - Karnofsky performance <70%
  - Portal fibrosis (moderate or severe)
  - Renal failure (GFR <30%)
  - Major intellectual impairment
  - Stage III or IV chronic sickle lung disease
  - Cardiomyopathy
  - HIV infection

Since the publication of trials using hydroxyurea, some of the recommendations have been modified, as recurrent pain and chest disease are probably now best treated initially with hydroxyurea, with BMT reserved for those patients who do not respond to hydroxyurea. The exclusions, however, are still relevant.

Recommendations

- All patients or families with a child with SCD should be offered the opportunity to discuss BMT as a treatment option. This should not depend upon the family having an available donor at the time. (C)
- BMT should be performed in centres experienced in transplants for haemoglobinopathies. Transplants from any donor other than HLA-identical family members should be undertaken only after careful consideration and extensive counselling by a team experienced in such work. Each SHT should have clear referral links to such a transplant centre. (C)

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Psychological management

Psychological issues for people with SCD and their families result mainly from the impact of pain and symptoms on their daily lives and society's attitudes to the condition and those affected.

There is considerable variability in how people with SCD cope with their condition. People with SCD experience different levels of health and such variations can lead to differences in psychosocial functioning. Some people cope relatively well, attend school or work and are active physically and socially. Their efforts should be recognised and encouraged where necessary. Others lead more limited and secluded lives. Nonetheless, this may not necessarily be a consequence of severe disease and the reasons should be sought and addressed.

Quality of life in people with SCD may therefore be lower than that of the general population, and with severe disease may deteriorate as people grow into adulthood. Children are also at greater risk of stroke with consequent impairment of their psychosocial functioning and cognition.

Studies on providing psychological therapy as a standard adjunct to routine medical management have shown encouraging results.[1] The overall goal is to help patients cope better, fulfil roles and achieve a better quality of life.

In addition there are specific indications for psychological intervention in the management of pain and stroke. A review of psychosocial interventions for pain and adherence outcomes[2] demonstrates that cognitive behavioural techniques are probably efficacious in treating sickle cell pain.

Psycho-education

Psycho-educational interventions primarily focus on improving knowledge and understanding of patients about their illness, while at the same time providing psychological support. Group interventions have been shown to identify issues and concerns in children and adolescents with SCD[3] and family interventions improve knowledge.[4] The rationale behind this approach is that information can lead to improved knowledge and better coping with the condition[5] and children who feel isolated may benefit from the support and motivation of others through shared experience.

Cognitive Behavioural Therapy

Cognitive Behavioural Therapy (CBT) comprises two psychological approaches: cognitive and behavioural techniques. The premise underlying CBT is that difficulties in living, relationships and general health have their origin in (and are maintained by) thoughts, emotions and behaviours.

The aim of cognitive interventions is to challenge and ultimately change inappropriate, self-defeating thoughts and allow the patient to lead a more productive and satisfying life. On the other hand, behavioural methods follow from the premise that inappropriate behaviours are learnt and therefore can be unlearnt.

CBT has been shown to reduce health service utilisation in both children and adolescents with SCD.[6] It has also been shown to reduce pain and improve mood and coping in adults.[7, 8]

Neuropsychology

Neurological complications in SCD result in both obvious and subtle neuropsychological deterioration. There is intellectual impairment with an increase in frontal-lobe problems of attention and executive functioning following overt stroke.[9] However, children who have silent infarct also experience learning and behavioural problems and are twice as likely to have school difficulties as other children.[10,11]

The Intercollegiate Working Party for Paediatric Stroke[12] recommends a detailed assessment of the child's cognitive and social functioning following a stroke. Although MRI can detect silent infarcts, it is impracticable to scan every child on a regular basis. However, there is evidence that neuropsychological screening provides a useful means of identifying those who may have suffered silent stroke.[13]

Recommendations

- All children and their families should have access to a clinical psychology service. (C)
- Cognitive behavioural therapy should be considered in addition to standard management in children experiencing frequent pain episodes. (C)
- A detailed neuropsychological assessment should be carried out in all children who have had a stroke and repeated annually. (C)
- Regular developmental assessments, neuropsychological screening or monitoring of school attainments in Standard Attainment Tests (SATs) should be carried out on a regular basis to assess for possible silent stroke. (C)

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Management of acute complications

General considerations

SCD is characterised by both acute and chronic complications. Acute complications will inevitably present initially to the local hospital (LHT) and may be associated with significant mortality in childhood. Mortality rates have been reduced through effective antimicrobial prophylaxis, parental education and appropriate acute intervention coordinated in dedicated sickle centres (SHT) employing experienced and well-trained staff.[1,2]

Recommendations

- Parents and carers should be made aware of the symptoms and signs associated with severe and life-threatening complications and know where to take their child if these occur. (C)
- A care pathway should be in place in the local unit (LHT) for assessment of the child in casualty, and for transfer to a designated ward if admission is necessary. (C)
- Protocols should be available to cover the management of all acute sickle cell complications. These should include worsening anaemia, febrile episodes, acute pain, acute neurological complications, acute chest syndrome and priapism. (C)
- A designated consultant paediatrician and/or paediatric haematologist should be responsible for the management of all children in the local hospital (LHT) and specialist sickle cell centre (SHT), with a named deputy. Junior doctors involved in assessment and treatment of acute sickle admissions should be made aware of acute complications and the local treatment protocols through regular education/training sessions. (C)
- Communication between the local centre (LHA) and expert opinion in the sickle cell centre (SHT) should be possible 24hrs/day for discussion of difficult cases and possible transfer of the patient. The means of communication should be made explicit. (C)
- Communication and transfer to a specified paediatric ITU should be readily available according to an agreed procedure. (C)

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Management of acute pain in hospital

Pain is the most common cause of acute morbidity in SCD and frequent hospital admission with acute pain has been associated with increased mortality.[1,2] Recurrent painful episodes have a negative psychological impact and the experience of poorly managed episodes in hospital, together with perceived negative attitudes of some staff, are often reported. These attitudes make it more difficult to develop effective long-term pain-coping strategies, and may lead to problematic behaviour on the ward.[3] There are UK guidelines

for pain management of SCD[4] and RCPCH guidelines on the recognition of acute pain in children in hospital.[5]

Validated pain assessment tools should be used to measure the child's self-report and behaviour.[6] These should include parental and healthcare professional assessment. Developmentally age-appropriate self-report tools should be used whenever children are able to participate.

Recommendations

- Pain assessment should include the use of a validated pain assessment tool that is developmentally age-appropriate. (C)
- There should be a policy in the A&E department regarding triage, pain assessment and length of acceptable time (not exceeding 30 minutes) from arrival to administration of analgesia. (C)
- Children should be managed according to a standard local analgesia protocol. This should be developed by collaboration between the local hospital (LHT) and sickle cell centre (SHT) and should include input from a pain control team, paediatric pharmacist and a paediatric anaesthetist designated for this purpose. The protocol should provide clear guidance on drugs, route of administration, dosage, and monitoring for analgesic effect and side effects. (C)
- Medical and nursing staff involved in treating children for acute pain should have regular training in pain management and in the application of the local analgesic protocol. (C)
- Children should be monitored regularly for effectiveness of analgesia and for signs of adverse effects (e.g. opiate-induced narcosis and hypoventilation, acute sickle chest syndrome etc). (C)
- The psychological needs of the child and family regarding coping with pain and avoiding sickle crises should be addressed during the admission. (C)

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Management of the febrile child

All children with sickle cell disorders are at increased risk of infection due partly to hyposplenism. In addition, defects in opsonisation and in cell-mediated immunity have been demonstrated. The risk is highest for the HbSS genotype, and in infants up to the age of 5. This is the time of particularly high risk for infection with encapsulated bacteria.

In the days before immunisation programmes and prophylactic antibiotics against Haemophilus influenzae and pneumococcus, infections with these bacteria were common and caused septicaemia, pneumonia and meningitis. Salmonella osteomyelitis, pneumonia due to typical and atypical organisms, and malaria, particularly in children returning from holidays in Africa, may also occur. Other infections, such as urinary tract infection and acute cholecystitis, are common. Parvovirus B19 causes temporary red cell aplasia. The reason for the increased susceptibility to salmonella osteomyelitis is not known.[1,2]

Diagnostic problems can occur. It is common for a child with a simple acute painful episode to present with a fever and no obvious evidence of infection. Some young children present with painful, swollen joints or areas of swelling in a long bone. In these cases, it may be difficult to differentiate between acute bone infarction due to sickling and an osteomyelitis or septic arthritis.

Blood cultures should always be taken, and if there is a high level of suspicion (e.g. high swinging fever, septic child, localized very tender swelling) imaging on ultrasound looking for subperiosteal fluid collection and surgical drainage should be considered before starting antibiotics.

Prophylactic penicillin should always be continued in hospital if a different antibiotic is not prescribed to treat an acute infection.

Empirical antibiotics should be given appropriate for the range of likely infectious agents. An agent active against pneumococcus should always be included. Cover for

suspected chest infection should include agents against atypical organisms.

Recommendations

- A protocol for antibiotic treatment of suspected or proven acute infection should be prepared by the SHT in collaboration with the local hospital (LHT) and with a designated paediatric microbiologist. (C)
- Cultures of blood, urine and other possible sites of infection should be routinely done on any child presenting with acute pain and fever. (C)
- Malaria films should be sent if there is any suspicion of malaria or if a patient has returned from a malarial region in the previous year. (C)

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Management of acute anaemia

The most common causes of an acute fall in haemoglobin of more than 2g/dl below steady-state haemoglobin level are acute splenic sequestration and temporary red cell aplasia (TRCA). This is usually due to parvovirus B19 infection.[1]

Acute splenic sequestration has been defined as an acute fall of haemoglobin and markedly elevated reticulocyte count, together with an acute increase in spleen size. It is a serious complication of SCD and, if unrecognised, carries significant mortality.[2] Mortality rates can be reduced substantially by parental education, regular palpation of the abdomen at home to detect early signs of splenic enlargement and prompt intervention with transfusion.[3,4] Recurrent splenic sequestration is an indication for splenectomy.

TRCA is characterised by a drop in haemoglobin over a period of about a week, often to levels as low as 3g/dl. It may be associated with fever, headache and abdominal pain. In a young child, it may be difficult to differentiate between TRCA and acute splenic sequestration, as the spleen may still be palpable. In contrast to acute splenic sequestration, the reticulocyte count will be very low or absent, and IgM for parvovirus B19 will be present. Recovery may be spontaneous, but a top-up transfusion is usually indicated.

Recommendations

- There should be a protocol for recognition and investigation of children presenting with pallor with or without pain in hospital. (C)
- Parents should be taught how to palpate for splenic enlargement and should be aware of the need to bring the child to hospital if they detect pallor and/or an enlarging spleen. They should be aware of the local procedure for emergency assessment. (C)
- Medical staff assessing children with acute sickle cell complications should be made aware of these complications through regular training/education sessions. (C)
- A local protocol for management, including indications for transfusion, should be available. (C)
- Children with two or more episodes of acute splenic sequestration should be considered for splenectomy. (C)

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Management of acute chest symptoms

The acute sickle chest syndrome is characterised by pleuritic chest pain, fever, abnormal chest examination and new pulmonary infiltrates on the chest X-ray. It is an important cause of morbidity and mortality in SCD.[1-3] It is particularly common in early childhood[4] although, at that time, the clinical features are generally more typical of pneumonia. In later childhood and adulthood, the syndrome can develop during a painful crisis or after anaesthesia.[5] Early intervention with an effective treatment protocol including analgesia, oxygen, physiotherapy, antibiotics and transfusion can significantly

reduce morbidity and mortality. A randomised controlled trial has shown that incentive spirometry performed regularly every 2 hours reduces the risk of acute chest syndrome in patients with chest and back pain.[6]

Recommendations

- Parents, patients and carers should be made aware of this complication. They should know how to recognise the symptoms and should be familiar with the local procedure for emergency assessment. (C)
- Children with chest pain, cough, respiratory distress, new chest signs or worsening hypoxia, presenting either in Accident & Emergency or during the course of a hospital admission, should be carefully assessed and monitored and a chest X-ray organised urgently. (C)
- Incentive spirometry should be used in children with acute chest and back pain. (A)
- Oxygen saturation monitoring should be used routinely, particularly in those children with respiratory signs and symptoms, acute pain affecting the trunk and girdle regions and those treated with opiates. (C)
- A local protocol should be prepared for management of the acute chest syndrome. This should include clear guidance on analgesia, observations, oxygen delivery, antibiotics, iv fluids, bronchodilators, physiotherapy, incentive spirometry and nursing observations. The indications for top-up transfusion, exchange transfusion and ventilatory support should be specified. There should also be a local protocol covering the practical issues of carrying out an exchange transfusion. (C)
- Medical and nursing staff should be made aware of this complication. Regular training and education sessions should advise on how to recognise it and provide updates on the local policy for management. (C)
- An agreement should be reached with the local paediatric intensive care unit about indications for transfer, means of communication and the protocol for treatment in the intensive care unit. (C)

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Management of acute neurological complications

(see also management of cerebrovascular disease, page 26)

Acute neurological complications are relatively common in children with HbSS and are potentially devastating. Cerebrovascular disease, particularly proximal vessel stenosis predisposes children to acute cerebral infarction. Occasionally older children present with subarachnoid or intracerebral bleeds, which may be related to single or multiple cerebral artery aneurysms. Acute neurological ischaemia is more likely to occur in children with pre-existing cerebrovascular lesions during acute anaemic events, or acute sickle cell crises.

Other acute neurological complications include behavioural changes, seizures and loss of consciousness. The causes of these complications are not always clear, even after extensive imaging.[1]

Symptoms suggestive of meningitis require urgent investigation, including lumbar puncture, blood culture and prompt antibiotic treatment. Acute ischaemic events require urgent investigation with CT and/or MRI scan to define the event and exclude a haemorrhagic component. This should be followed by exchange transfusion as soon as possible to reduce the risk of progression of the lesion. Intracerebral or subarachnoid bleeds defined by such imaging may need to be followed by lumbar puncture (if safe) and, in some situations, surgical intervention.

Although stroke in a child with SCD is likely to be secondary to cerebrovascular pathology, it is important to remember that stroke in childhood can result from alternative pathology, particularly a source of cardiovascular emboli. These should be actively excluded. The Royal College of Physicians, with the paediatric stroke working party, has published guidelines on the management of all causes of acute stroke in childhood.[2]

Recommendations

- Each SHT should have access to a designated paediatric neurologist who can assess and advise on acute neurological complications. (C)
- Each SHT should have a clear plan for access to a neurosurgical unit for managing children and adolescents with cerebral haemorrhage and subarachnoid bleeds. (C)
- RCP guidelines on the management of acute stroke should be followed and specific guidelines for acute stroke in SCD should be prepared by the SHT for the local unit (LHT). (C)
- Each SHT should have access to neuroimaging facilities including paediatric CT, MRI/MRA, and EEG. (C)

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Management of fulminant priapism

(see also page 29)

Priapism is a sustained, painful and unwanted erection. A prolonged attack, lasting more than 3 hours should be treated as a surgical emergency as, if untreated, cavernosal fibrosis and impotence may ensue. The condition becomes more common in adolescence and minor attacks may go unreported due to reluctance to tell parents or healthcare professionals.[1]

Minor attacks may be aborted by emptying of the bladder, taking a warm bath and use of oral analgesia. Frequent minor attacks or 'stuttering priapism' may be treated with oral etilefrine.[2]

A prospective study of 15 young patients showed that aspiration and irrigation with dilute epinephrine produced immediate detumescence in 37 out of 39 occasions.[3] Etilefrine may also be used.[4] In the event that this is not successful, a glans-corporal shunt may need to be performed and if no relief occurs the urologists may need to go on to perform a bilateral non-parallel spongiosum corporal shunt or a corporal-venous shunt.[5]

Blood transfusion may be indicated as part of the overall management if a shunt needs to be performed.

Recommendations

- A policy for the management of severe fulminant priapism should be drawn up with the SHT and a paediatric urology team. (C)
- All boys and their carers should be aware of the policy and know how to access emergency treatment. (C)
- Aspiration and irrigation with etilefrine or ephedrine should be the initial treatment of choice. (C)

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Appendix 1 - Writing group membership of the First Edition (September 2006)

The initiative for this document came from the British Committee for Standards in Haematology with backing from the UK Forum on Haemoglobin Disorders, the NHS Sickle Cell and Thalassaemia Screening Programme and the Sickle Cell Society.

Members were invited to join the writing group to represent areas of high and low prevalence of sickle cell disease; the disciplines of paediatrics, haematology, nursing, general practice and psychology; parents; and the voluntary sector. All the writers have extensive experience in managing sickle cell disease and work in areas of high prevalence. In addition, commentators with less direct experience were included to ensure relevance for the whole country. Two people were also members of the writing group for the standards for the clinical care of children and adults with thalassaemia in the UK (UKTS 2005) to provide consistency where there was overlap in the management of the two conditions. There has been no external funding and there is no declared conflict of interest.

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The document has been circulated to a wide range of stakeholders including members of the UK Forum on Haemoglobin Disorders, members of the Sickle Cell Society, paediatricians and haematologists in proposed SHT centres and other clinicians known to have an interest in the subject.

Acknowledgments

Marcus Bankes, Charles Buchanan, Annabel Crowe, Baba Inusa, Jane Logan, Jean Mullen, Ade Olujohungbe, Keith Pohl, Elene Psiachou-Leonard, Irene Roberts, Maureen Scarlett, Cecilia Shoetan, Anne Yardumian and Olu Wilkey.

Writing group membership of this Second Edition (October 2010)

As this second edition has mainly consisted of making a small number of updates to the first edition, together with adding other relevant documents and material from the detailed guidance, it seemed most efficient for the lead author, Dr Moira Dick, to agree changes and to seek confirmation from various experienced clinicians, in particular Dr David Rees and Dr Phil Darbyshire. Patient and family/carer views were put forward by Dr Asa'ah Nkohkwo of the Sickle Cell Society.

Dr Allison Streetly and Dr Elizabeth Dormandy contributed to the revisions in so much as they affected screening and arrangements for transition into care. The NHS Sickle Cell and Thalassaemia Screening Programme also provided secretarial and administrative support.

Again, there has been no external funding and there is no declared conflict of interest.

Appendix 2 - Methodology and literature search strategy

These guidelines were formulated in accordance with the principles specified by the Appraisal of Guideline Research and Evaluation (AGREE collaboration, www.agreecollaboration.org). The writing group (see Appendix 1 for membership) began by constructing a list of headings and topics. These were divided and allocated to individual members on the basis of their interest and expertise. Where the group had no particular expertise, e.g. orthopaedics or endocrinology, relevant clinicians were asked to contribute on those topics.

A search of Medline, Embase and the Cochrane Controlled Trials Register was carried out to ensure complete coverage of the evidence on which the recommendations are based. Relevant guidelines (e.g. the British Committee for Standards in Haematology, Royal College of Paediatrics in Child Health, National Institutes of Health, USA and the National Service Framework for Children) were consulted. Members of the writing group brought their own expertise and knowledge of the literature. Recommendations from the National Service Framework for Children were taken into account.

Levels of evidence

Wherever possible, recommendations draw on published research. Although there is a wealth of clinical experience in paediatric sickle cell disease, there is a lack of prospective, randomised controlled trials to inform these guidelines. However, an evidence base does exist in two main areas: prevention of pneumococcal infection; and screening for cerebrovascular disease.

Against this background, the writing group has used a range of sources including published retrospective analysis of clinical data and non-randomised, non-controlled intervention, expert opinion and the views of patients and their families.

Grading of recommendations

Grade type based on Agency for Health Care Policy & Research (AHCPR 1992) recommendations:

A
(levels 1a, 1b)
Requires at least one randomised trial as part of the body of literature of overall good quality and consistency addressing the specific recommendations.

B
(levels 1a, 1b, III)
Requires availability of well-conducted clinical studies, but no randomised clinical trials on the topic of the recommendations.

C
(level IV)
Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

Literature search strategy

Sources searched: Medline, Embase, Cochrane Controlled Trials Register

Dates of search: January 1980 to August week 2, 2006

OVID Medline

1. exp Hemoglobinopathies/
2. exp Hemoglobin, Sickle/
3. (hemoglobinopath$ or haemoglobinopath$).tw.
4. sickle cell.tw.
5. sickle-cell.tw.
6. meniscocytic.tw.
7. drepanocytosis.tw.
8. (hemoglobin s or haemoglobin s).tw.
9. (hemoglobin sc disease or haemoglobin sc disease).tw.
10. (sickling and (blood or plasma)).tw.
11. 1 or 2 or 3 or 4 or 5 or 7 or 9 or 10

Combined with RCT strategy below:

1. RANDOMIZED CONTROLLED TRIAL.pt.
2. CONTROLLED CLINICAL TRIAL.pt.
3. Randomised Controlled Trials/
4. Random Allocation/
5. Double-Blind Method/
6. Single-Blind Method/
7. 1 or 2 or 3 or 4 or 5 or 6
8. Animals/
9. Humans/
10. 8 not 9
11. 7 not 10
12. CLINICAL TRIAL.pt.
13. exp Clinical Trials/
14. (clin$ adj25 trial$).ti,ab.
15. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
16. Placebos/
17. placebo$.ti,ab.
18. random$.ti,ab.
19. Research Design/
20. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 20 not 10
22. 20 not 11
23. 11 or 22

Appendix 3 - Summary of aims and objectives of NHS Sickle Cell and Thalassaemia Screening Programme – newborn sickle cell screening

More information available at http://sct.screening.nhs.uk.

Programme aims:

- To achieve the lowest possible childhood death rate and to minimise childhood morbidity from sickle cell disorders.

Overall outcome to be achieved at national level:

- Mortality rate in children under 5 of less than 4 per 1000 person-years of life (2 deaths per 100 affected infants) by 2010.
- To accurately diagnose infants born with specific conditions where early intervention is likely to be beneficial (HBSS, HbSC, HbSD, Hb/β thalassaemia (β+, β^0, δβ, Lepore), $HbSO^{Arab}$, HbS/HPFH.

Programme objectives

- To offer screening for sickle cell disorders to all infants.
- To process tests in a timely manner.
- To identify and arrange timely follow-up of infants identified as needing further investigation.
- To ensure effective and acceptable follow-up, care and support for affected infants and their carers.
- To offer treatment and start parental education in a timely manner.
- To minimise the adverse effects of screening – including failure to follow up screen-positive infants, inaccurate or inadequate information, unnecessary investigation and follow-up, and inappropriate disclosure of information and failure to communicate results to parents (normal and carrier).
- To ensure that responsibility, accountability and performance management for all aspects of the programme are clear and that these link together from local to national level and between the newborn and antenatal programme.

Outcome measures

Outcome	Criteria	Minimum standard (core)	Achievable standard (developmental)
Best possible survival for infants detected by the programme.	Mortality rates expressed in person-years.	Mortality rate in children under 5 of less than four per 1000 person-years of live (two deaths per 100 affected children).	Mortality rate in children under 5 of less than two per 1000 person-years of life (one death per 100 affected children).
Accurate detection of all infants born with major clinical significant abnormality.	Sensitivity of the screening programme. High quality newborn laboratory services.	99% for HbSS 98% for HbSC 95% for other variants	99.5% for HbSS 99% for HbSC 97% for other variants

Appendix 4 - Specialised Services National Definitions Set (number 38) for sickle cell and thalassaemia

Extracted from the website August 2010 - http://www.ncg.nhs.uk/index.php/key-documents/specialised-services-national-definitions-set/

SPECIALISED SERVICES NATIONAL DEFINITIONS SET (THIRD EDITION)

Specialised Haemoglobinopathy Services (all ages) - Definition No. 38

Preface

This definition is part of the third edition of the Specialised Services National Definitions Set (SSNDS) published in 2010. The second edition of the SSDNS (containing 35 definitions) was published in 2002.

The third edition of the SSNDS contains 34 definitions (4 definitions have been dropped and 3 new definitions have been added). Each definition has been updated or created by an inclusive process involving providers (clinicians, hospital managers, and information and coding staff), commissioners and patients' groups. Every effort has been made to ensure that each definition contains all the relevant medical condition and treatment classification codes as well as referencing key policy and standards documents. The final version of each definition has been approved by the National Specialised Commissioning Group (NSCG) and endorsed by the relevant professional organisations. The third edition definitions are available from the NSCG website: www.specialisedcommissioning.nhs.uk .

The 10 Specialised Commissioning Groups, acting on behalf of their member PCTs, are responsible for commissioning arrangements for specialised services. The purpose of a definition is to identify the activity that should be regarded as specialised services. A service is specialised if the planning population (i.e. catchment area) for that service is greater than one million people. This means that a specialised service would not be provided by every hospital in England; generally, it would be provided by less than 50 hospitals.

The definitions are not prescribed service models nor do they set service standards. Where national standards for a specialised service already exist, these may be referred to in the definition. Inclusion of a treatment or intervention in a definition should not be taken to mean that there is established evidence of clinical or cost effectiveness.

The content of individual definitions in the SSNDS will inevitably change over time as new healthcare services which are specialised are introduced into the NHS and other services, which were previously specialised, become commonplace and cease to be considered specialised. The SSNDS will be regularly reviewed and further editions will be produced in the future. Definitions may also be updated on an individual basis if that is appropriate.

Future editions of the SSNDS will become more refined as the classifications systems develop and become better able to categorise specialised service activity. The current classification systems used in the third edition are the International Classification of Diseases, version 10, and the OPCS Classification of Interventions and Procedures, version 4.5.

Queries and suggestions for possible improvements should be sent to the NSCG's email address at: enquiries@nsscg.nhs.uk.

1. Introduction

This definition focuses on people with thalassaemia major, sickle cell disease (SCD) and other rare inherited anaemias. There are about 800 patients with thalassaemia and 15,000 with SCD in England. A large number are under 19 years of age. SCD is one of the commonest inherited conditions in England; around 300 babies are born in England each year with SCD compared to 20-30 babies with thalassaemia.

SCD predominantly affects black and African-Caribbean people, whilst thalassaemia affects Asian and Mediterranean peoples. The prevalence varies according to geographical area, being highest in urban ethnic populations, particularly London, where about two-thirds of SCD patients live.

SCD and thalassaemia are complex disorders, and although often grouped together and managed by the same specialist team, their clinical manifestations and treatments are different. Treatment for children also differs significantly from adolescent and adult care. All SCD affected children born in England, and the majority with thalassaemia, will be identified by the neonatal screening programme, now fully implemented in England. Life expectancy for both conditions is progressively improving and is likely to be more than 50 years. Maximising quality of life is an important factor in the organization of care and in treatment decisions. Further, other very rare anaemias requiring lifelong transfusion and chelation (e.g. Blackfan Diamond anaemia and congenital sideroblastic anaemia) fall within the spectrum of this definition.

Sickle Cell Disease

SCD includes the genotypes HbSS, HbSC, HbS beta thalassaemia, and several rarer combinations including HbSD and ,HbSO. Homozygous SCD (HbSS) accounts for about 70% of patients and is clinically the most severe of the common genotypes. SCD is a complex condition characterised by bouts of severe and occasionally life-threatening acute illness (crises), increased susceptibility to specific severe infections, chronic fatigue, delayed growth and progressive tissue and organ damage. SCD patients are intermittently unwell, and severely affected patients miss large amounts of school and find it difficult to sustain employment. Management includes prophylaxis against infection; treatment of pain; expert management of acute, life-threatening complications; monitoring and treatment of chronic complications; and education and psychosocial support for patients and carers. About 10-20% of children and a smaller percentage of adults require regular blood transfusions, together with iron chelation therapy.

Beta Thalassaemia Major

Beta Thalassaemia major (Thalassaemia in future text refers to all Thalassaemic states) causes severe anaemia, bone expansion and failure to thrive in infancy and these patients require regular blood transfusions, usually starting between 6 months and 2 years of age, every 3 to 4 weeks for life. Iron accumulates as a result of regular blood transfusions, and if not removed (chelated), will cause damage to endocrine glands, liver and heart, with death from heart complications in the second or third decade. Good organization and monitoring of transfusions, together with safe and effective iron chelation therapy are the medical goals of a thalassaemia service combined with education and psychosocial support for patients and carers to minimize disability and optimize quality of life.

Thalassaemia Intermedia

Thalassaemia intermedia is less common than thalassaemia major and is usually due to inheritance of milder thalassaemia genes. Thalassaemia intermedia encompasses a wide range of conditions including mild Beta + Thalassaemia, Haemoglobin H disease and Beta Thalassaemia in combination with HbE. There is variable anaemia and bone expansion but regular transfusions are not required during childhood. Some adolescents will require transfusion, either because of poor growth, absent pubertal development, or complications due to bone marrow expansion. A larger proportion will eventually require transfusion in adulthood because of the long-term effects of chronic anaemia.

2. Rationale for the service being included in the Specialised Services National Definitions Set

These are complex conditions which involve a holistic approach from a wide range of disciplines offering care in a clinical network covering three levels: community, local and specialist teams. The clinical network is co-ordinated by the specialist centre as recommended in the three publications listed in Paragraph 6. Inadequate care results in avoidable morbidity and mortality in childhood and early adult life. The national antenatal and neonatal screening programme which now covers all of England was instituted to avoid such problems, however early morbidity and mortality is still seen in children coming into the country from areas with less developed health services .

Critical aspects of management need specific facilities and equipment as well as staff possessing knowledge and experience. This is the case not only for management of acute complications, but also the supervision and monitoring of long-term therapy to avoid chronic complications. Continuing advances in treatment, complex treatment decisions, new drugs and investigations are best supervised by a specialist working in a specialist centre attending to a large number of patients each year.

3. Links to other services in the Specialised Services Definitions Set

No. 2	Specialised services for blood and marrow transplantation (all ages)
No. 4	Specialised services for women's health
No. 5	Assessment and provision of equipment for people with complex disabilities (all ages)
No. 7	Specialised rehabilitation services for brain injury and complex disability (adult)
No. 8	Specialised neurosciences services (adult)
No.11	Specialised renal services (adult)
No.13	Specialised cardiology and cardiac surgery services (adult)
No.18	Specialised services for infectious diseases (all ages)
No.19	Specialised services for liver, biliary & pancreas medicine and surgery (adult)
No.20	Medical genetics services (all ages)
No.22	Specialised mental health services (all ages)
No.23	Specialised children's services
No.24	Specialised dermatology services (all ages)
No.26	Specialised rheumatology services (all ages)
No.27	Specialised endocrinology services (adult)
No.29	Specialised respiratory services (adult)
No.31	Specialised pain management services (adult)
No.34	Specialised orthopaedic services (adult)

4. Detailed description of specialised haemoglobinopathy services activity

Levels of Care for SCD and Thalassaemia

Services for SCD and thalassaemia are provided in specialist haemoglobinopathy centres, in local hospitals and in the community. These three levels of care are described in more detail in Appendix 1.

The prevalence of rare inherited anaemias varies around the country from high prevalence areas such as London, where two-thirds of SCD patients live, to low prevalence areas where there are relatively few residents who are from high-risk ethnic groups. Local hospitals in high-prevalence areas have large caseloads of patients with SCD and thalassaemia, but local hospitals in low-prevalence areas may only have a handful of patients; these two types of local hospital will have very different levels of knowledge and expertise.

Consequently in high-prevalence areas the local hospital is likely to provide much of the day-to-day care and look to the specialist centre to provide certain outreach services and joint clinics, whereas in low-prevalence areas the local hospital is more likely to refer patients to the specialist centre. However all local hospitals will need to provide prompt, effective and safe management of uncomplicated acute painful SCD episodes and follow appropriate protocols for pain management in emergency departments and in-patient environments.

Paragraphs 4.1 to 4.9 set out the services which are provided by the specialist centre within a clinical network and also details those services that can be delivered, as described in the national standards documents, by local hospitals and in the community.

4.1 Supervision of blood transfusion management of SCD and Thalassaemia and exchange transfusions for SCD

Acute exchange transfusions are required for certain severe complications of SCD and are best done in a specialist centre, where either manual exchange or automated exchange (erythrocytapheresis) may be used. If the patient is too unwell to travel or needs the transfusion urgently, the exchange can be done in the local hospital after liaison with the specialist centre.

The specialist centre supervises the blood transfusion management of the patient; this includes decisions about initiating regular transfusion, annual monitoring of transfusion therapy, adjustment of the regime, more complex transfusion procedures such as exchange transfusion and use of intravenous access devices (e.g. Port-a-cath). Supervision of regular transfusion requires good communication between the specialist centre, the local hospital and the patient/carer as well as maintenance of a patient-held record.

Chronic transfusion therapy is not a specialised service and should be done in the local hospital close to the patient's home or work provided appropriately qualified staff are available. It entails regular hospital attendances every 3-4 weeks and each episode may last at least 4-8 hours. The majority is straightforward top-up transfusions, but some patients with SCD will have exchange transfusion, which is technically more demanding.

4.2 Supervision of iron chelation management in SCD and Thalassaemia, prescribing iron-chelating drugs, monitoring and adverse event management and optimization of compliance

Complications of long-term transfusion in thalassaemia and SCD include:

- endocrine dysfunction
- liver disease
- cardiac disease.

Death in early adulthood has been a common outcome due to inadequate control of cardiac iron overload. Complications due to iron overload can be prevented by iron chelation therapy. The standard modality is given as a home therapy by the patient/carer who administers a subcutaneous infusion over 8-12 hours, 5-6 times per week, for life. It is a particularly demanding regime requiring sustained lifelong adherence for effective control of iron stores with sustained patient support and encouragement to ensure adequate compliance.

There are now three licensed iron chelating drugs: deferoxamine (aka desferrioxamine) (given by subcutaneous infusion), deferiprone (orally administered) and deferasirox (orally administered). All of these drugs are expensive and have significant side effects. The overall supervision of the patient resides with the specialist centre and will cover: choice of drug, monitoring for efficacy and side effects, dose adjustments and changes to the chelation regime although shared care arrangements may be applied for ongoing monitoring.

4.3 Prevention and management of neurological complications of SCD including Transcranial Doppler screening in childhood, specialised neuroradiology, neurology and neuropsychology services

Neurological complications of SCD include:

- Recurrent severe headaches
- seizures
- transient ischaemic attack
- stroke (ischaemic or haemorrhagic)
- central nervous system infections.

Defects in cognitive functioning and poor school performance are common in childhood, and are often associated with clinically silent cerebral ischaemic lesions which can be demonstrated in about 20% of children with SCD (HbSS, homozygous SCD genotype) by magnetic resonance imaging (MRI) brain scan.

Clinically apparent (overt) ischaemic stroke is seen in about 10% of children. Transcranial Doppler (TCD) screening is a non-invasive method of identifying children at risk. All children with HbSS and other severe phenotypes will require annual TCD scanning from the age of 2, with abnormal and borderline investigations (seen in about 25%) repeated frequently and investigated with MRI/MRA scans. TCD scans are done by an experienced sonographer (i.e. experienced nurse, doctor or radiographer) under the direct supervision of the specialist centre and subject to a quality assurance system.

The stroke risk is about 30-40% in those with abnormal scans (time-averaged mean velocity in the internal carotid, middle cerebral or anterior cerebral artery of over 200 cm/sec). In such cases a long-term regular transfusion programme will reduce the risk of stroke by over 90%.

Neurological symptoms and abnormal or inadequate TCD scans are investigated by MRI and magnetic resonance angiography (MRA) of the brain. These scans reveal a complex spectrum of ischaemic and cerebrovascular damage, whose evaluation and treatment requires specialist expertise.

Haemorrhagic stroke is seen in adolescents and young adults. It is a common cause of death in this age group. The aetiology is not clear, and currently there is no proven primary or secondary preventive management.

Children and adults who have had a stroke are usually managed with long-term transfusion to prevent recurrence. They may be severely disabled and need full access to all rehabilitation modalities. The specialist centre will need to develop pathways of care for these patients involving hospital and community agencies including specialised rehabilitation services.

4.4 Management of severe and life-threatening acute complications of SCD and Thalassaemia

Acute complications in SCD

The most severe episodes with life-threatening acute complications will be treated by the specialist centre, these include:

- fulminant sepsis
- acute sickle lung syndrome
- acute splenic or hepatic sequestration
- ischaemic and haemorrhagic stroke
- subarachnoid haemorrhage
- acute renal failure
- multi-organ failure
- biliary obstruction
- fulminant priapism
- post-transfusion hyperhaemolysis
- acute ophthalmological complications (e.g. complications of sickle retinopathy/central retinal artery occlusion)
- osteonecrosis of major joints (e.g. hip, shoulder)

In these cases, management is extremely challenging since there are features of these acute events which resemble general medical emergencies, yet the management may be very different. Exchange transfusion, intravenous analgesia, inhaled oxygen, mechanical ventilation and/or CPAP, incentive spirometry, careful attention to fluid balance and appropriate choice of antibiotics all form part of the management.

If these patients cannot be transferred to a specialist centre, the specialist centre will need to advise the local hospital, provide protocols for management of such cases and monitor treatment.

Specific therapy for severe and complicated SCD cases

The introduction and supervision of drugs (e.g. hydroxycarbamide) to prevent or mitigate sickle crises and pain is specialised although the day to day monitoring of the blood count may be devolved to a local unit. On

rare occasions regular blood transfusion programmes are recommended to alleviate severe recurrent sickle pain or other emerging specific organ dysfunction; again the institution and supervision of these programmes is specialised even if the transfusion is delivered locally.

Acute complications in Thalassaemia Major include:

- heart failure and cardiac arrhythmias
- post-splenectomy sepsis
- iron chelator therapy-associated sepsis
- acute endocrine disturbances (e.g. hypocalcaemic tetany)
- acute hepatic decompensation.

Acute complications are uncommon in thalassaemia, but need to be recognized and treated urgently usually within the specialist setting or in close liaison with the centre. These patients are iron loaded and may have impaired immunity and impaired cardiac and endocrine function, potentially leading to decompensation during intercurrent illness and a rapidly progressive and fatal outcome. The treatment of heart failure in thalassaemia is unique to this condition. General physicians will be unfamiliar with the spectrum of acute infections emphasizing the need for specialist involvement.

Uncomplicated SCD crises

All local hospitals will manage the more severe SCD crises requiring expert hospital management with strong opiate analgesia, good hydration, antibiotics and occasionally transfusion. Adverse effects of opiates are common and patients need to be monitored closely to ensure sustained effective analgesia and minimization of side effects until the pain settles and the opiate analgesia can be withdrawn. Prompt, effective and safe management of simple acute painful episodes aims to avoid or minimise hospital admissions. Such treatment will be provided in every local hospital. Specialist centres may support local hospitals in developing protocols for pain management in emergency departments and in-patient environments, as well as providing training for local hospital staff.

The commonest acute complication is the painful SCD crisis which is generally **managed at home** with support from family and other regular carers and community services input as appropriate. These crises result in time lost from school and work and may have severe psychosocial effects on the whole household.

4.5 Management of chronic complications of SCD and Thalassaemia

Regular monitoring will detect early evidence of complications which can occur during childhood, adolescence and adulthood, and tend to accumulate with age, resulting in significant disability and reduced life expectancy. Prevention and treatment requires specialist knowledge and experience, close collaboration with other specialties (usually through regular joint clinics) and monitoring protocols agreed between the specialist centre and the local hospitals which can be implemented throughout the network. Within these networks the diagnosis and management of chronic complications is the responsibility of the specialist centre, but the day to day delivery of protocol based treatments can be undertaken at the local hospital in collaboration with the specialist centre.

Chronic complications of SCD cover a wide range due to irreversible and often progressive tissue damage including:

- stroke
- chronic sickle lung syndrome
- pulmonary hypertension
- chronic renal impairment
- avascular necrosis of the hips, spine and shoulders
- retinopathy
- chronic ankle ulceration.

Chronic complications in Thalassaemia include:-

- endocrine dysfunction (growth hormone deficiency, hypogonadotrophic hypogonadism, hypothyroidism, hypoparathyroidism, diabetes which may require insulin treatment)
- cardiac dysfunction
- chronic liver disease (cirrhosis, portal hypertension, hepatic failure, hepatocellular carcinoma, often associated with transfusion-transmitted hepatitis B or C)
- bone problems (avascular necrosis, osteoporotic fractures of the hips and spine, disc disease).

Most of these complications are due to chronic iron overload and can be reduced by sustained effective chelation, although bone disease has a complex and poorly understood aetiology.

Chronic complications in Thalassaemia Intermedia include:

- gallstones
- ankle ulceration
- iron overload
- pulmonary hypertension
- thrombosis
- retinal damage
- pseudoxanthoma
- bone problems (avascular necrosis, osteoporotic fractures of the hips and spine, disc disease)
- chronic pain.

4.6 Surgical management of SCD and Thalassaemia

Surgery will be carried out in a specialist centre by surgeons and anaesthetists who have experience in treating SCD and thalassaemia patients working closely with the haematology or paediatric haematology specialist.

Children and adults with SCD and thalassaemia frequently require surgery and are high risk as they can develop acute sickling complications during the peri-operative period and are more likely to develop other surgical complications such as infection and haemorrhage. There are special requirements for oxygenation, hydration, analgesia and pre-operative transfusion support.

The commonest surgical procedures include:

- adenotonsillectomy
- splenectomy
- cholecystectomy (usually laparoscopic)
- hip replacement
- Port-a-cath insertion.

4.7 Management of pregnancy in SCD and thalassaemia

Each year in the UK 40-50 women with SCD will become pregnant as will 4-5 women with thalassaemia major. These are high risk pregnancies which ideally are managed in a joint high-risk antenatal clinic by the specialist in SCD and thalassaemia together with an obstetrician who has particular expertise in this area. Decisions about treatment during pregnancy and mode of delivery are made on an individual basis. There is significant maternal mortality in both conditions, with one maternal death in the UK every one or two years.

SCD tends to become more severe during pregnancy, with a higher frequency of painful crises in the later stages, and an increased risk of severe complications such as acute chest syndrome. There is also an increased risk of intrauterine growth restriction, early delivery and miscarriage. The perinatal mortality rate in babies of women with SCD is 4 times the national rate.

Thalassaemic women are often hypogonadic and require fertility treatment in order to conceive. The risks for the pregnancy depend largely on the state of iron overload. Transfusion and chelation treatment will need to be modified during the pregnancy to avoid complications for the mother and the fetus. Fetal outcomes for women with thalassaemia major are usually good.

The Human Fertilisation and Embryology Authority now allows embryo testing and selection for an human leukocyte antigen (HLA) matched, non-thalassaemic, non-SCD embryo to be able subsequently to allow haemopoeitic stem cells from umbilical cord blood to be collected at birth for transplantation into an affected sibling. This is a combined service from specialised IVF, genetic and haematology services.

4.8 Stem cell transplantation for SCD and Thalassaemia

Both SCD and thalassaemia can be cured during childhood by allogeneic stem cell transplantation, but this requires a histocompatible sibling for stem cell donation. In November 2008 there are two centres in the UK which have built up a large experience in allo-stem cell transplantation for haemoglobinopathies (Birmingham Children's Hospital and St Mary's Hospital, London).

(see Definition 2. Specialised Services for Blood and Marrow Transplantation (all ages))

4.9 Out-patient review of SCD and Thalassaemia

Annual review The annual review should be undertaken by a specialist, either in an outreach clinic or in the specialist centre itself. The aim of the annual review is to obtain an overview of the condition and its treatment over the previous year and should be undertaken in line with existing standards documents. The annual review can follow a standard format with some parts of the review best done by a nurse specialist and others by a medical specialist.

The specific information needed to inform the annual review will depend on the patient concerned and may include reports from other specialties, including neurology (SCD), cardio-respiratory (SCD), musculoskeletal (SCD and thalassaemia) and gastrointestinal (SCD and thalassaemia).

Routine monitoring Routine out-patient monitoring is required every 3 months for thalassaemia and every 3-6 months for SCD depending on age and complications. In the case of thalassaemia, this is for the monitoring of haemoglobin (Hb) level, adjusting the transfusion regime and optimising iron chelation therapy through assessment of adherence, efficacy and adverse effects. In the case of SCD this is to monitor symptoms, the frequency of crises and adherence to medication and for parental education and advice on life-style and crisis avoidance. If the SCD patient is being treated with hydroxycarbamide or transfusion, this requires regular monitoring and adjustment as necessary. These 3-6 monthly monitoring visits are not considered a specialised service.

5. Identifying and costing specialised haemoglobinopathy services activity

5.1 Existing currencies:

- Out-patient attendances
- Out-patient procedures
- Non face to face out-patient attendances
- Day cases
- In-patients
- Healthcare resource Groupings (HRGs)

5.2 Existing classification systems:

- ICD diagnostic codes (see table below)

D560	Thalassaemia	Alpha thalassaemia
D561	Thalassaemia	Beta thalassaemia
D562	Thalassaemia	Delta-beta thalassaemia
D563	Thalassaemia	Thalassaemia trait
D564	Thalassaemia	Hereditary persistence of fetal haemoglobin (HPFH)
D568	Thalassaemia	Other thalassaemias
D569	Thalassaemia	Thalassaemia, unspecified
D570	Sickle-cell disorders	Sickle-cell anaemia with crisis
D571	Sickle-cell disorders	Sickle-cell anaemia without crisis
D572	Sickle-cell disorders	Double heterozygous sickling disorders (Hb-SC, Hb-SD, Hb-SE)
D573	Sickle-cell disorders	Sickle-cell trait
D578	Sickle-cell disorders	Other sickle-cell disorders
D582	Other hereditary haemolytic anaemias	Other haemoglobinopathies

The ICD10 diagnostic codes in the above table identify haemoglobinopathy conditions. Please note that both the specialist centre and the local hospital may use some of these diagnostic codes and hence the codes cannot be used to specifically identify specialised haemoglobinopathy services.

- OPCS – 4.5 procedure codes

See "Haemoglobinopathies OPCS" worksheet in "SSNDS Definition No.38 Specialised Haemoglobinopathy (all ages) website codes" spreadsheet.

5.3 Costing activity

Please refer to the latest Department of Health Guidance on Payment by Results for up to date information on national tariffs and activity included/excluded from tariff.

Please note that not all the Payment by Results inclusions and exclusions listed below are specialised activity, but they are included here for completeness.

(i) Is in scope of 2010/2011 Payment by Results and thus has a national tariff:

- Clinical haematology first/follow-up and single/multi-professional : multi-discplinary out-patients attendances (Treatment Function Code : 303) – MANDATORY TARIFF
- Non face to face out-patient attendances (for TFCs that have a mandatory tariff for face-to-face out-patient attendances) – NON MANDATORY tariff
- Out- patient procedures – MANDATORY tariff for 49 procedures only
- Admitted patient care –
  - MANDATORY combined tariff for day case and ordinary elective in-patient spells
  - MANDATORY separate tariff for 17 day case and for 18 elective in-patient spells
  - MANDATORY tariff for ordinary non-elective spells

(ii) Is excluded from 2010/2011 payment by Results and therefore requires a locally negotiated tariff:

- Services
  - Critical care services (adult)
  - Nationally commissioned services
- Out-patient attendances – see list of specific exclusions
- Admitted patient care – see list of specific exclusions
- Drugs – see list of specific exclusions

5.4 Outstanding issues raised regarding currencies and classification systems

It is unclear whether the current Payment by Results tariff adequately captures the range of activity and hence costs of a long term condition such as haemoglobinopathy disease.

Various approaches to costing activity are being considered by the national haemoglobinopathy sub-group including a banding system, whereby a tariff is created for the average costs of a year's care and reflecting levels of complexity and intensity.

6. National Standards and Guidelines

Available from: www.sct.screening.nhs.uk :

- NHS Antenatal and Newborn Screening Programme (2006) 'Sickle Cell Disease in Childhood: Standards and guidelines for clinical care'
- NHS Sickle Cell and Thalassaemia Screening Programme (March 2009) 'Transcranial Doppler Scanning for Children with Sickle Cell Disease – Standards and Guidelines'
- McLeod C. et al (2009) 'Deferasirox for the treatment of iron overload associated with regular blood transfusions (transfusional hemosiderosis) in patients suffering with chronic anaemia ' Health Technol Assess vol.13(1) pp1-144

Available from www.sicklecellsociety.org :

- Sickle Cell Society (2008) 'Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK'

Available from www.ukts.org :

UK Thalassaemia Society (Revised 2008 edition) 'Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK'

Endorsement

British Society for Haematology
DH Haemoglobinopathies Clinical services Development Group

Appendix 1: Levels of Care for Sickle Cell Disease and Thalassaemia

Care of sickle cell disease and thalassaemia patients usually takes place within a clinical network and can be divided into three levels of care.

Specialist team care includes:

- Institution and supervision of blood transfusion management (SCD and thalassaemia)
- Institution and supervision of iron chelation management, prescribing of iron chelating drugs, monitoring, adverse event management and

optimization of compliance (SCD and thalassaemia)

- Prevention and management of neurological complications of SCD including Transcranial Doppler screening in childhood, specialised neuroradiology, neurology and neuropsychology services (SCD)
- Management of severe and life-threatening acute complications (SCD and thalassaemia)
- Management of chronic complications (SCD and thalassaemia)
- Surgical management (SCD and thalassaemia)
- Management of pregnancy (SCD and thalassaemia)
- Bone marrow transplantation (SCD and thalassaemia)
- Annual out-patient review (SCD and thalassaemia)
- Outreach clinics in local hospitals (SCD and thalassaemia).

Local team care includes:

- Management of acute, uncomplicated crises (SCD)
- Routine monthly day case transfusions (thalassaemia major and transfusion-requiring SCD)
- Routine out-patient monitoring (SCD and thalassaemia)
- Agreed shared care arrangements for specific therapies (SCD and thalassaemia) (including support with adherence to iron chelation regimes, monitoring of hydroxycarbamide, care following stem cell transplantation).

These functions are generally undertaken by hospital-based haematology or haemoglobinopathy nurse specialists and a designated paediatrician/haematologist.

Community care includes:

- Education of and support to patients and carers in self management of these long-term conditions
- Support to patients and carers in home management of milder sickle cell crises and supervision after discharge from hospital
- Education of and support to patients and carers in adherence with home medication (oral penicillin prophylaxis for SCD, regular iron chelating therapy for patients with thalassaemia major and for patients with SCD on regular transfusion)
- Liaison with and facilitation of access to community health services, social services, educational services, welfare benefits etc.
- Support for local users' groups.

These functions may be undertaken by specialist haemoglobinopathy nurses. They may be based in a local community setting (e.g. Community Sickle Cell and Thalassaemia Centres already exist in some high prevalence areas, especially in London) and liaise with local hospital or specialist centre clinics. Alternatively, in some areas hospital-based specialist nurses provide outreach services to the community from the local hospital or specialist centre clinic. In both scenarios there is close collaboration with the hospital-based paediatrician/haematologist who is responsible for SCD and thalassaemia care.

Haemoglobinopathies OPCS worksheet

OPCS codes for Definition 38. Specialised Haemoglobinopathy Services (all ages) (3rd edition)

OPCS-4.5 CODE	OPCS-4.5 Category	OPCS-4.5 Sub-Category
X321	Exchange blood transfusion	Neonatal exchange blood transfusion
X322	Exchange blood transfusion	Exchange of plasma (single)
X323	Exchange blood transfusion	Exchange of plasma (2 to 9)
X324	Exchange blood transfusion	Exchange of plasma (10 to 19)
X325	Exchange blood transfusion	Exchange of plasma (>19)
X326	Exchange blood transfusion	Red cell exchange
X327	Exchange blood transfusion	Leucopheresis

OPCS-4.5 CODE	OPCS-4.5 Category	OPCS-4.5 Sub-Category
X328	Exchange blood transfusion	Other specified
X329	Exchange blood transfusion	Unspecified
X331	Other blood transfusion	Intraarterial blood transfusion
X332	Other blood transfusion	Intravenous blood transfusion of packed cells
X333	Other blood transfusion	Intravenous blood transfusion of platelets
X334	Other blood transfusion	Autologous peripheral blood stem cell transplant
X335	Other blood transfusion	Syngeneic peripheral blood stem cell transplant
X336	Other blood transfusion	Allogeneic peripheral blood stem cell transplant
X338	Other blood transfusion	Other specified
X339	Other blood transfusion	Unspecified includes: intravenous blood transfusion NEC
X341	Other intravenous transfusion	Transfusion of coagulation factor
X342	Other intravenous transfusion	Transfusion of plasma NEC
X343	Other intravenous transfusion	Transfusion of serum NEC
X344	Other intravenous transfusion	Transfusion of blood expander
X348	Other intravenous transfusion	Other specified
X349	Other intravenous transfusion	Unspecified
X902	High cost haematology and nutrition drugs	Hypoplastic haemolytic and renal anaemia drugs, Band 2

Appendix 5 - Extract from Sickle Cell & Thalassaemia: Handbook for Laboratories 2nd edition; September 2009

Issuing Laboratory Reports

The parents and GP should be informed of all outcomes of screening. The approach adopted should follow general guidance from the UK Newborn Bloodspot Programme Centre (www.newbornscreening-bloodspot.org.uk).

Laboratories are responsible for sending all screening results to Child Health departments or their equivalent in a timely manner. This information will be used to assess coverage of the screening programme and to provide a mechanism for reporting 'normal' results to parents and other healthcare professionals. Presumptive positive results should be reported immediately by the laboratory to the designated healthcare professional.

Annual data returns

A timely annual data return will be required from all newborn screening laboratories using the template that has been developed in conjunction with the UK Newborn Bloodspot Programme Centre. This will request data on sickle cell screening as well as the other screening tests performed on the newborn bloodspot. See http://newbornbloodspot.screening.nhs.uk/datacollection.

Action required for particular categories of results

Infants with sickle cell disease:
Results should be sent by the laboratory as a matter of urgency (fax/electronically, etc) to the designated healthcare professional, and confirmation of receipt documented. Parents should be informed by personal contact. Copies of all reports should be sent to the GP and health visitor.

Infants found to have a condition other than sickle cell disease which requires follow-up:
Results should be sent by the laboratory to designated healthcare professional and confirmation of receipt documented. Parents should be informed by personal contact. Copies of all reports should be sent to the GP and health visitor.

Infants heterozygous for a haemoglobin variant:
Results should be sent by the laboratory to the designated healthcare professional and confirmation of receipt documented. Parents and GP should be informed by a locally agreed mechanism.

Infants with no abnormality detected:
Results should be provided in written form by the child health department or equivalent for the parents of the child and the child's GP.

Follow-up procedures

Infants with sickle cell disorders:
Diagnostic testing should be undertaken before 2 months of age. Parental samples (where required) should be tested at the same time. Samples for diagnostic testing for sickle cell disease should be sent to a specialist laboratory which has expertise in haemoglobinopathy analysis in the newborn period.

Other clinically significant conditions:
Diagnostic testing (when required) should be undertaken before 2 months of age and it is recommended that parental samples should also be tested at the same time. Samples should be sent to a specialised laboratory which has expertise in haemoglobinopathy analysis of infants.

Carriers of common haemoglobin variants (Hb S, C, D^{Punjab}, E):
Using screening techniques, second line testing can confirm the presumed identity of the haemoglobin variant and it should not be necessary to take a further blood sample. Carriers are usually asymptomatic, but carriers of Hb S can be at risk under particular high stress situations. It is helpful if their families are made aware of their carrier status and screening of parents offered if their results are not fully documented.

Rarer haemoglobin variants:
Most of these will be infants who are heterozygous for the rarer variants and will have no clinical or haematological manifestations. However, some rare variants, particularly unstable haemoglobins or those with altered oxygen affinity, can produce clinical manifestations even in heterozygotes, although not all of these will be detected by screening. Local policies should be in place for the follow-up of these babies. If it is decided to establish the identity of the variant, further samples on the neonate and/or parents should be referred to a **laboratory with expertise in haemoglobin analysis and its clinical significance**. It may be easier to test parental samples at this stage rather than re-bleed the neonate, although it must be realised that such results may be misleading in cases of non-paternity or

of de novo mutations. Once the nature of the condition is established, medical follow-up can be provided if necessary

Transfused babies

The presence of transfused blood in the neonate will interfere with the interpretation of the results from the haemoglobin analysis of the bloodspot and possibly invalidate the results. It should be policy in all neonatal units to take a bloodspot specimen for sickle cell screening prior to giving a transfusion whenever possible. A technique of analysing DNA extracted from the white cells from the bloodspot has been developed to overcome the complications caused by the presence of transfused blood on the bloodspot card. This service is being funded for two years from autumn 2009 by the NHS Sickle Cell and Thalassaemia Screening Programme and is provided by King's College Hospital and Sheffield Children's Hospital. It must be emphasized that this service does not obviate the need to take a pre-transfusion specimen wherever possible.

The DNA test will detect the presence of the sickle haemoglobin gene and is able to differentiate between babies with only the sickle gene present; those with the sickle gene and another haemoglobin gene and those with no sickle gene present. All babies in whom the sickle gene is detected should be referred for clinical follow-up. This test does not confirm the identity of the non-sickle haemoglobin and if the parents are known to be at risk of another haemoglobinopathy, they may wish for further standard haematology tests to be carried out on their baby. This is not considered part of the newborn screening programme and should be initiated in a clinical setting. Testing using standard haematology laboratory techniques should not normally be undertaken until at least four months after the last transfusion.

Premature infants

Hb A is normally detectable by 30 weeks gestation and is sometimes detected by 24 weeks. Results from premature infants should be interpreted with caution. Premature infants who show no Hb A need repeat testing to check for the presence of a sickle cell disorder or ß-thalassaemia major.

Quality assurance

The non-cancer screening programmes are developing a quality assurance framework that will operate across the antenatal and newborn programmes. This framework covers the screening journey from offer of testing through to entry into care, as well as user experience, equity, governance and commissioning.

There are also programme-specific quality assurance processes. The quality improvement minimum and achievable standards are given in detail in the NHS Sickle cell and Thalassaemia Screening Programme: Standards for the linked antenatal and newborn screening programme (http://sct.screening.nhs.uk/cms.php?folder=2493).

For newborn sickle cell screening, besides the minimum criteria for laboratories given below, these include:

- Minimum standards for sensitivity of the screening test:
  - 99% detection for HbSS
  - 98% detection for Hb SC
  - 95% detection for other variants
- IT capacity to support standard reporting and audit requirements of the Programme
- Production of an annual report of process and outcome to ensure the laboratory is meeting the Programme's aims and objective.
- Failsafe arrangements to be in place. For laboratories this includes checking all samples have been received and all results are received and acted upon (positive and negative) in a timely manner, including links made to previous screening results.
- Review of all screen positive results
- At least an annual meeting to review linkage of the antenatal and newborn screening programmes and to report areas for development.

In August 2008, the UK Newborn Screening Programme Centre published 'Standards andGuidelines for Newborn Blood Spot Screening' (http://newbornbloodspot.screening.nhs.uk/standards). The nine standards it contains are based on the original 6 standards published in 2005 and aim to drive improvement in the quality of the bloodspot sample and the timeliness of re-screening. The 'core standards' set out the expected level of performance to deliver an acceptable level of quality. The 'developmental standards' depict a level of performance that delivers enhanced quality. The standards are accompanied by a number of best practice guidelines which should be followed to deliver high quality screening processes and to meet the standards.

Timeliness

Bloodspot card samples should be taken 5-8 days after birth (ideally on day 5), sent to the laboratory within 24 hours of being taken and received in the screening laboratory within 4 working days of being taken (see UK Newborn Bloodspot Screening Programme Centre guidance – Standards 3 and

4). The report should be sent by six weeks of age to enable arrangements to be made so that affected children can be immunised with pneumococcal vaccine by eight weeks and attend a specialist clinic by 12 weeks of age.

NHS numbers

The bloodspot card should have the baby's NHS number to ensure correct identification and confirm coverage of the programme, and ideally the mother's NHS number to allow linkage with antenatal records.

Reports

The recommendations made in the 'Reporting results for the newborn screening programme' section should be followed.

Storage of bloodspot cards

Laboratories will be expected to comply with the 'Code of Practice for the Retention and Storage of Residual Spots' published in the Policies and Standards of the UK Newborn Screening Programme Centre.

Minimum Laboratory Criteria for Newborn Screening

1. The laboratory must be appropriately accredited with a nationally approved accreditation scheme such as Clinical Pathology Accreditation UK (Ltd), now formally part of the United Kingdom Accreditation Service (UKAS).
2. The workload of the newborn screening laboratory should exceed 25,000 specimens per year (ideally 50,000), to give appropriate economies of scale and confidence in the interpretation of abnormal results.
3. There must be a senior member of the laboratory staff at medical consultant or clinical scientist consultant level responsible for the haemoglobinopathy screening service, with defined lines of accountability and authority for all laboratory aspects of the service.
4. The initial screening test must be performed using high performance liquid chromatography (HPLC), isoelectric focusing (IEF) or a method giving comparable results with a confirmatory test for positive results being performed on the original blood spot, using a different technique from the initial screening test.
5. Screening laboratories must use the appropriate screening status codes when interfacing with the child health record systems and must collect the recommended data fields for the annual return required for monitoring and audit purposes.
6. There must be a documented risk management policy for the laboratory aspects of the haemoglobinopathy screening service. This should describe the steps in the testing protocol where mistakes could occur and the procedures that have been implemented to minimise the risk of the mistake occurring.
7. The laboratory must participate in an accredited External Quality Assessment Scheme (EQAS), appropriate for newborn screening (e.g. NEQAS) and must be able to demonstrate satisfactory performance as defined by the criteria specified by the EQA scheme organisers.
8. Appropriate internal quality control procedures must be undertaken and documented, e.g. recording of reagent lot numbers, recording of turnaround time for reports, results of internal quality control specimens, etc.
9. The laboratory must participate in audit at local and regional level, with the results of the newborn screening programme being published in a local annual report. There must be links established with the antenatal screening laboratories to audit the effectiveness of both arms of the neonatal screening programme.
10. The laboratory must be willing to release information on screening performance to any appropriate monitoring group of the National Screening Committee and the NHS Sickle Cell and Thalassaemia Screening Programme Centre, and be open to peer review visits and inspection by the commissioners or their representatives at any time, by mutual agreement.

Lines of responsibility

The midwife is responsible for:

- Informing the parent(s) or guardian of the reasons for testing.
- Providing relevant information to parents.
- Offering the test, collecting the dried bloodspot sample 5-8 days after birth, labelling and sending off the sample by the appropriate transport system as soon as it has been taken.
- Obtaining informed consent or written notification if the parents wish to opt out of testing.
- Taking repeat specimens when requested by the laboratory.

The screening laboratory is responsible for:

- Documentation of the infant's demographics, specimen analysis and issuing of results within a timely manner after receipt of the sample.

- Reporting non-normal results to the designated healthcare professional responsible for informing the parents and for the follow-up of affected infants.
- Reporting all results to the relevant child health department.

The designated healthcare professional with relevant skills and training is responsible for:

- Informing parents of the results and arranging clinical follow-up of infants with sickle cell disease.
- Informing parents of the results and arranging clinical follow-up of infants with other potentially clinically significant conditions.
- Ensuring that infants are not lost to clinical follow-up before registration in a clinic.
- Providing information and counselling for the parents of infants who are carriers or have other benign conditions detected.
- Arranging repeat testing as indicated by the laboratory.

The child health department is responsible for:

- Checking that all newborn babies are offered screening.
- Recording the results of screening in the child health record.
- Disseminating the normal results.
- Ensuring babies without results are offered testing.

Support services

Clinical network arrangements:
It is recommended that the screening laboratory is part of a managed clinical network, with a recognised specialist/ regional centre and a named specialist, for annual review of all affected infants. A process to formalise existing informal networks is being developed with support from the Department of Health and relevant professional groups, including the British Society of Haematology, the UK Haemoglobinopathy Forum, the Royal College of Paediatrics and Child Health and other interested parties including Specialist Commissioners. There is now a National Definitions Set for Specialised Haemoglobinopathy Services.

Support services for timely follow-up and treatment need to be in place and coordinated across the area covered by a programme to ensure that the potential benefits of the programme are realised. Experience from the USA shows that the main reason for the failure of a screening programme in terms of clinical outcomes is failing to ensure that identified infants are registered in a programme of treatment and care or failing to identify that having been registered, they are subsequently lost to follow-up.

Specific arrangements for counselling women and their partners with an affected infant need to be in place for all areas covered by a newborn screening programme.

Failsafe arrangements:
Each local area needs to have fail-safe arrangements in place, with designated individuals responsible from the relevant professional disciplines. These are distinct from the care pathway for individual users of the service and also from the responsibilities of individual professionals in following up particular actions for individual patients.

For the newborn programme this includes having a system to ensure that there is a review of screen-positive infants, together with the success of enrolling them in appropriate follow-up care and starting them on a defined programme of treatment with a relevant local service provider (and a recognised specialist unit, as appropriate).

For both the newborn and the antenatal programmes, working together as a linked programme, this includes a requirement for a formal independent process, such as a regular audit meeting, for the review of all screen-positive results and action taken to follow up screen-positive cases. This should be undertaken on a regular basis at least annually, with specified individuals involved and clear accountability to ensure that processes of care operate smoothly and in a timely manner.

Appendix 6 - Networks of clinical care

Region	Newborn Screening Lab	SHT Network Centres with associated local hospitals
East of England	Cambridge Great Ormond Street	East of England Trusts now linked into North Middlesex London network
East Midlands	Sheffield	**Nottingham** **Leicester** Associated local hospitals: Derby, Kettering and Northampton (adults)
London		
East London & Essex	Great Ormond Street	**The Royal London** Associated local hospitals: Barking Havering & Redbridge, Whipps Cross Hospital, Basildon, Newham, Homerton, Mid Essex at Chelmsford , Princess Alexandra Hospital at Harlow, Colchester and Southend
North East London	Great Ormond Street	**North Middlesex Hospital/Great Ormond Street** Associated local hospitals: Chase Farm at Enfield, Princess Alexandra at Harlow, Addenbrookes at Cambridge, King's Lynn, Norfolk and Norwich, Ipswich
North Central London	Central Middlesex	**University College Hospital/ Whittington Hospital** Links to many trusts particularly for tertiary thalassaemia review
North West London	Great Ormond Street Central Middlesex	**Central Middlesex** **Imperial (St Mary's Hospital & Hammersmith)** Associated local hospitals: Ealing Hospital, West Middlesex at Isleworth, Hillingdon Hospital, Northwick Park, plus outside the Brent area looser links with Luton, Milton Keynes and Watford
South London	King's/GSTT	**King's College Hospital, London** **Guy's and St Thomas's Hospital (GSTT)** **University Hospital Lewisham** Associated local hospitals: Mayday Hospital at Croydon (paeds), Queen Mary's Sidcup, Queen Elizabeth Hospital at Woolwich, Brighton and other SE Coast hospitals including Medway, Dartford and Farnborough
South West London	St Helier	**St George's Hospital** Associated local hospitals: St Helier, Mayday (mainly adults), Royal Surrey at Guilford, East Surry at Redhill, St Peter's Hospital at Chertsey
Northeast and Yorkshire & Humberside	Newcastle Leeds Sheffield	**St. James' Hospital, Leeds** **Sheffield** Associated local hospitals: Bradford, South Tees (James Cook Hospital) plus Newcastle & NE

Region	Newborn Screening Lab	SHT Network Centres with associated local hospitals
North West	Manchester Liverpool	**Manchester Children's Hospital** **Alder Hey Children's Hospital** Associated local hospitals : Blackburn (Queen's Park), Lancaster, Tamesidew
South Central	Oxford Portsmouth	**Configuration yet to be confirmed** Hospitals in Region: Milton Keynes, Royal Berkshire Hospital at Reading, The John Radcliffe Hospital at Oxford, Southampton (including Basingstoke and Portsmouth)
South East Coast	Various	All trusts now linked to either Royal London (mainly Essex) or South London via King's or GSTT
South West	Bristol	**Bristol Royal Infirmary** Local: Derriford Hospital, Plymouth (low prevalence area)
West Midlands	Birmingham	**Birmingham Children's** Associated local hospitals: Sandwell, Wolverhampton, Coventry, University Hospital of N. Staffs at Stoke, (Northampton and Kettering paeds)

Appendix 7 - Data collection by clinical networks to support monitoring of newborn outcomes

The NHS Sickle Cell and Thalassaemia Screening Programme assess the outcomes of the linked antenatal and newborn screening programme at a national level. For babies affected with sickle cell or thalassaemia the following are assessed:

- mortality and morbidity up children affected by haemoglobinopathies, up to age 5
- timely entry of affected babies/children to care
- a look back at the mothers antenatal screening history

To obtain reliable data on these outcomes requires named data on all babies with sickle cell disorder or thalassaemia. Collecting named data without consent is a sensitive issue. The Programme has received approval from the Ethics and Confidentiality Committee of the National Information Governance Board (http://www.nigb.nhs.uk/ecc/register-1/register-of-approved-applications) for this work. We are also working closely with the Sickle Cell Society and the UK Thalasaemia Society to ensure the work addresses user's views. More information about this work is available at http://sct.screening.nhs.uk/evaluation.

The Ethics and Confidentiality Committee of the National Information Governance Board have balanced the autonomy of individuals with the importance of assessing the outcomes of a screening programme. They have given approval for one year in the first instance and have asked the programme to consider how to assess newborn outcomes without named data. Therefore the Programme are setting up two data collection systems on babies with sickle cell disease or thalassaemia: named and anonymous. Both named and anonymous data are based on the programme standards, and are requested as one record per baby. Data will be requested on an annual basis, based on financial years. An Access database to store these results is available on request. The table below lists the anonymised data items required. The table also indicates whether these items are included in the named data collection. Details of named data collection is available at http://sct.screening.nhs.uk/evaluation.

Eligibility: All children requiring long term follow up for sickle cell diseases identified by the age of five years, regardless of screening history will be included.

Sickle cell conditions to include: HbSS, HbSC, HbS beta thalassaemia, Hb S/D ^{Punjab}; HbS/O^{arab}, Hb-S/HPH/HbSE

Standard and Objective	Minimum Standard	Data to collect	Specific Data items (one record per baby)	Notes
Newborn O1: Best possible survival for infants detected with a sickle cell disorder by the screening programme	Mortality rate from sickle cell disease and its complications in children under five of less than four per 1,000 person years of life (two deaths per 100 affected children	Date of Death if applicable Cause of death if applicable	Patient ID (unique and anonymous) Year of birth Date of Death Cause of Death	full date full date free text **(also in named data collection)**
Newborn 2i: Accurate detection of all infants born with major clinically significant haemoglobin disorders	99% detection for HbSS 98% detection for HbSC 95% detection for other variants	Screen result, confirmed result and methods used , if available	Newborn screening result Confirmed result Methods used to confirm result	FS, FSC, FS-Other, FE, F-only (also in **named data collection**) As listed in Tables 1 and 2 of laboratory handbook **(also included in named data collection)**

Standard and Objective	Minimum Standard	Data to collect	Specific Data items (one record per baby)	Notes
Newborn P4: Effective follow up of infants with positive screening results (sickle cell disorder) – all babies to be registered with a local clinic/centre	90% attend local clinic by three months of age	Age of baby when first attend local clinic	Age of baby when confirmed results documented in appropriate notes Age of baby when first attended local clinic	Age in weeks, recorded in electronic or paper notes in local or specialist centre Age in weeks (also **included in named data collection**)
Newborn P5: Timely confirmation of diagnosis for infants with a positive screening result	90% of cases of Hb SS and Hb SC have confirmation of result documented in clinical notes by six months of age	Age of baby when confirmed result documented in appropriate notes		
Newborn P6i: Timely effective treatment and education for: Hb-SS, Hb-SC, Hb-SD –Punjab, Hb-βThalassaemia, Hb-So ^{Arab}, Hb-S/HPH	90% offered and prescribed Penicillin V or alternative by three months	Age of baby when penicillin prescribed Vaccination status at aged 6 months	Age of baby when penicillin prescribed Vaccination status Information offered at first visit with named HP	Age in weeks **(also included in named data collection)** **(also included in named data collection)** 2, 4, 13, 24 months Yes / No
Newborn P6ii: Communication to parents	95% of families offered information on condition, follow up, and treatment at first visit with named professionals.	Information offered at first visit with named HP	Yes/ no response	
Newborn S1ii: Up-to-date registers maintained of babies (cases) for which units are responisible	Less than 10% of cases on registers who have been lost to follow up within the past year.	Number of babies lost to follow up in past financial year, if available	Lost to follow up	Yes / No
		Antenatal screening result including PND result, if available		**(also included in named data collection)**

*Age could be calculated from date of birth and date event took place if these data are available

There are links between this work and that of the National Haemoglobinopathy Registry (see Appendix 8)

Appendix 8 - National Haemoglobinopathy Registry

Introduction

The National Haemoglobinopathy Registry (NHR) is a registry of patients with red cell disorders (mainly sickle cell disease and thalassaemia major) living in the United Kingdom, the central aim of the registry is to improve treatment services. It is an important initiative linked to the attempt at quality improvement by providing basic information on numbers of patients with these disorders, treatment regimes (e.g. access to Doppler scan - prevention of stroke) and relevant medication (e.g. hydroxyurea to prevent crises). The NHR also functions as a real-time national surveillance network collecting data on complications seen (e.g. stroke, heart failure, deaths, etc.) and transfusions received.

The expectation is that the Registry will in the long term provide basic and important demographic and therapy-related data of value to clinicians, user groups and commissioners. The continued collection of accurate data about patient numbers, distribution and therapy is vital for service design and planning.

Using the NHR

Registering for an account

To register for an account on the NHR, for security reasons you must be connected to the secure NHS internal network (e.g. within an NHS site). To register, simply visit the NHR website (www.nhr.nhs.uk), click the link to log into the NHR system and complete the new user request form. You will then be validated by the NHR support team and allocated an account on the NHR.

Obtaining patient consent

It is important to note that no patient should be registered onto the NHR without first obtaining their informed consent. To facilitate this, an information leaflet has been produced which is accessible from the NHR website. The information leaflet should be shown to the patient so that they are able to make an informed choice as to whether they wish their data to be entered onto the NHR.

Requested data

The NHR collects information on diagnosis, date of birth, GP code, NHS number, name, the use of blood transfusion, therapy types, and the risk factors for some of the disease complications such as use of iron chelation therapy. The database also collects information on adverse events such as stroke, ITU admission, clinically significant bacteraemia, cardiac events and causes of death. A complete list of captured data items can be viewed on the NHR website.

Entering data

For entry of data to the NHR database, a user-friendly, secure online network system has been created using the latest technologies. The system has been written with speed and ease of use as key objectives and as such registrations can take as little as two minutes per patient. A helpline is also available if any problems are experienced in use of the system.

Reports

The NHR publishes aggregated anonymised reports on the data held. Data is presented at the national annual meeting which is held in November. Details of these meetings are posted on the NHR website. Basic data on numbers of patients and therapy are also published on the NHR website and in newsletters.

Who manages the NHR?

The database is managed by the Steering Group of the NHR which includes representation from all key stakeholders. These include representatives from the DH, UK Thalassaemia Society, Sickle Cell Society, NHS Sickle Cell and Thalassaemia Screenng Programme, leading haemoglobinopathy clinicians, health commissioners and representation from the UK Forum.

If you require further information in relation to the NHR please contact the NHR support team at support@mdsas.com or 0161 277 7917

Appendix 9 - Clinical peer review quality requirements - paediatric

Quality Requirements for Health Services Caring for Children and Young People with Haemoglobinopathies

Version 1.1, October 2009
Review by: December 2012

Introduction

These Quality Requirements have been developed to support implementation within services for children and young people of the *'Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK'* and *'Sickle Cell Diseases in Childhood: Standards and Guidelines for Clinical Care'*[1]. They reflect the aims, standards and guidelines of both documents. They also support the principles of the National Service Framework for Children, Young People and Maternity Services[2]. The Quality Requirements do not cover the national screening programme and its immediate follow up procedures but it has been agreed that peer review visits will also look at compliance with screening standards P3, P4, P5 (p29), S1i and S1ii (Appendix 1). The Quality Requirements apply only to the care of children and young people and therefore do not cover the aspects of the *'Standards and guidelines for clinical care'* which relate to adult patients only. At a later stage, the Quality Requirements may be extended to cover the care of adult patients.

Standards and guidance can be interpreted in different ways and may not always be implemented in full. These Quality Requirements clarify the arrangements that should be in place and provide the answer to the question: "For each service, how will I know that the 'Standards and Guidelines for Clinical Care' have been implemented?" The Quality Requirements are suitable for use in self-assessment or peer review visits. As with the Standards documents, these Quality Requirements describe what services should be aiming to provide. All services should be working towards meeting all applicable Quality Requirements within the next two to five years.

Development of the Quality Requirements took place during 2006 and early 2007 through a sub-group of the UK Forum on Haemoglobinopathy Disorders. The suitability of the Quality Requirements for use in peer review was tested in a pilot visit to the Royal London Hospital in January 2007.

[1].Sickle Cell Diseases in Childhood - Standard and Guidelines for Clinical Care (2006) is available on the publications section of the NHS Screening website: www.sickleandthal.org.uk . Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK (2005) is available in the downloads section of the UK Thalassaemia website: www.ukts.org .

[2].Department of Health, National Service Framework for Children, Young People and Maternity Services. 2004

Structure of the Quality Requirements

Topics: The Quality Requirements (QRs) are divided into the following topics:

- Specialist and Local Haemoglobinopathy Teams (SHT / LHT)
- Commissioners of services

More detail of the functions of each type of service is given in the *Standards for the Clinical Care of Children and Adults with Beta Haemoglobinopathy in the UK'* and *'Sickle Cell Diseases in Childhood: Standards and Guidelines for Clinical Care'*.

Some services will treat mainly children and young people with either sickle cell disease or thalassaemia and some Quality Requirements – or parts of Quality Requirements – are therefore applicable only to sickle cell disease only (SC) or thalassaemia only (T). Some teams will care for patients with all types of haemoglobinopathy and will be expected to meet both 'SC' and 'T' Quality Requirements. Quality Requirements relating to the care of patients with thalassaemia are also applicable to teams treating children and young people with sickle cell disease who need regular transfusion.

Specialist Haemoglobinopathy Teams may also provide local care for some patients.

Responsibilities

- Commissioners of services are responsible for achieving QRs 52 and 53 – with advice from providers of services for children and young people with haemoglobinopathies.
- Responsibility for achieving QRs 7 to 19 is shared between commissioners and providers of services (in particular, senior management within provider Trusts).
- QRs 1 to 6 and 20 to 51 are the responsibility of the nominated lead consultants and nurses (QRs 7, 9, 11 and 12), working in cooperation.

Sections: Each Quality Requirement has the following sections:

Reference number	This number is unique to these Quality Requirements and is used for all cross-referencing within the Quality Requirements. The section also indicates the type of team to which each Quality Requirement is applicable.
Quality requirement	This describes the standard that hospital Trusts and specialist commissioning arrangements are expected to meet.
Demonstration of Compliance	This describes how organisations may show that they are meeting the Quality Requirement. This is not prescriptive. Organisations may have other ways of showing that they meet the requirement.
Notes	The notes give more detail about either the interpretation or the applicability of the Quality Requirement.

Abbreviations:

LHT Local Haemoglobinopathy Team
SHT Specialist Haemoglobinopathy Team
SC Sickle cell disease
T Thalassaemia

Ref	Quality Requirement	Demonstration of Compliance
SPECIALIST AND LOCAL HAEMOGLOBINOPATHY TEAMS		
Information and support for patients and their carers		
1 LHT SHT	Written information should be offered to patients and their families covering at least: 1 A simple explanation and description of the condition, how it might affect the individual, possible complications and treatment. For sickle cell disease this information should include: a Problems, symptoms and signs for which emergency advice should be sought b How to manage pain at home, including how to avoid pain, and non-pharmacological interventions c Importance of adequate fluid intake d Use of antipyretics for fever e Importance of regular antibiotics and full immunisation f How to feel the spleen and its significance. For thalassaemia this information should include: a Problems, symptoms and signs for which emergency advice should be sought b The importance of maintaining good haemoglobin levels by transfusion c Potential problems of iron load and how it can be managed. 2 Details of the services available locally including: a Clinic times and how to change an appointment b Key contact name and number c Alternative contact if key contact away d Who to contact for advice out of hours e How to use emergency services f Ward usually admitted to and its visiting times g Community services and their contact numbers h Details of support groups available. 3 Health promotional material including a Inheritance and implications for other family members b The importance of a good diet and regular exercise c Implications for travel d Age appropriate information on avoiding smoking and excess alcohol consumption e Age appropriate information on contraception and sexual health f Where to go for further information, including useful websites and national voluntary organisations.	Examples of written information available Notes: *1 Information may be from a recognised, published resource such as 'Sickle cell disease – a guide for parents' / 'What is thalassaemia', or a local document.* *2 Information available should relate to the disease type/s treated by the team.* *3 Information should be available in formats and languages appropriate to the needs of the patients. This may include large print and taped information.* *4 Age-appropriate information as well as information for parents should be available.* *5 Information may be given at different stages in the patient's care, as appropriate.*

Ref	Quality Requirement	Demonstration of Compliance
2 LHT SHT	Examples of written information available Written information for the patient's primary health care team should be available covering at least: a All aspects of QR1 b The need for regular prescriptions, penicillin and analgesia (SC)	Examples of written information for primary health care teams *Note: The information on regular prescriptions, penicillin and analgesia may be in the form of a clinic letter or additional information*
3 LHT SHT	Information should be available on transition to adult care. This information should cover all aspects of the transition (QR43	Examples of age-appropriate information for young people and information for parents.
4 LHT SHT	The SHT and its linked LHTs should have agreed a patient-held record for recording at least: a Information about the patient's condition b Current management plan c Regular medication d Named contact for queries and advice e Alternative contact for times when key contact is away.	Example of patient-held record. *Note: Although responsibility for achieving this QR is given to the SHT, LHTs should cooperate with the SHT in the development and agreement of the patient-held record.*
5 LHT SHT	The locally agreed patient-held record (QR4) should be in regular use within the LHT / SHT.	Discussion with staff and patients. Examples of completed records.
6 LHT SHT	Services should be provided in a child friendly environment, including toys and books / magazines for children and young people of all ages.	Facilities available
STAFFING and SUPPORT SERVICES		
7 LHT SHT	The LHT should have a nominated lead paediatrician / paediatric haematologist with responsibility for guidelines, protocols, training, audit relating to haemoglobinopathies, liaison with community services and overall responsibility for liaison with the SHT. The lead consultant should undertake CME activity of relevance to care of children and young people with haemoglobinopathies	Name of lead paediatrician / paediatric haematologist. Record of relevant CME activities. *Note: The lead paediatrician may be community or hospital-based.*
8 LHT SHT	There should be agreed arrangements for cover for absences of the lead paediatrician.	Details of cover arrangements *Note: Cover arrangements may be a second paediatrician within the LHT OR may be guidelines, agreed with the SHT, for contacting the SHT for advice.*
9 LHT SHT	The SHT should have a nominated lead paediatrician / paediatric haematologist consultant with an interest in the care of patients with haemoglobinopathies who should have responsibility for guidelines, protocols, training, audit relating to haemoglobinopathies and overall responsibility for liaison with referring LHTs. The lead consultant should undertake CME activity of relevance to care of children and young people with haemoglobinopathies.	Name of lead consultant. Record of relevant CME activities. *Note: The lead consultant may also have responsibility for liaison with community services for patients for whom local care is provided.*
10 LHT SHT	The lead consultant (QR9) should have a named deputy who will provide cover for absences. The named deputy in the SHT should undertake CME activity of relevance to care of children and young people with haemoglobinopathies.	*Name of deputy.* *Record of relevant CME activities.*

Ref	Quality Requirement	Demonstration of Compliance
11 LHT SHT	The LHT should have a lead nurse who has responsibility, with the lead consultant (QR7), for guidelines, protocols, training, audit relating to haemoglobinopathies, liaison with community services and liaison with the SHT. The lead nurse should have specific training in the care of patients with haemoglobinopathies.	Name of lead nurse and details of relevant training. *Note: The lead nurse may be community or hospital-based.*
12 LHT SHT	The SHT should have a lead haemoglobinopathy nurse with responsibility, with the lead consultant (QR9), for guidelines, protocols, training, audit relating to haemoglobinopathies and liaison with referring LHTs. The lead nurse should have specific training in the care of patients with haemoglobinopathies.	Name of lead nurse and details of relevant training. *Note: The lead nurse may also have responsibility for liaison with community services for patients for whom local care is provided.*
13 LHT SHT	The SHT should have a nurse specialist or counsellor who provides outreach support for patients in the community. This nurse specialist / counsellor should have specific training in the care of patients with haemoglobinopathies.	Name of nurse specialist or counsellor and details of relevant training.
14 LHT SHT	There should be agreed cover arrangements for the outreach nurse specialist / counsellor.	Details of cover arrangements
15 LHT SHT	Access to the following staff and services should be available: a MRI and CT scanning b Transcranial Doppler ultrasonography (SC) c Hospital dental services d Genetics services e Bone marrow transplantation services f Contraception and sexual health services g Consultant cardiologist h Consultant endocrinologist i Consultant hepatologist j Consultant neurologist k Consultant ophthalmologist l Consultant orthopaedic surgeon m Consultant obstetrician n Child and adolescent mental health services	Details of services available *Notes:* *1 SHTs should ensure access to an appropriate level of specialist expertise in the care of patients with haemoglobinopathies. This may be through services within the same Trust or through cooperation with other Trusts or SHTs. It should be indicated where each service is available to children attending the unit, if not on site.* *2 Some services may also be available within LHT facilities.*
16 LHT SHT	The following services should be available a Paediatric high dependency care b Paediatric intensive care There should be agreed criteria for admission to each level of care.	Details of services available. Criteria for admission. An audit of admissions to high dependency and intensive care is a desirable additional demonstration of compliance. *Note: Where high dependency or intensive care services are located on a different hospital site to the haemoglobinopathy service, details of transfer arrangements should also be available.*

Ref	Quality Requirement	Demonstration of Compliance
17 LHT SHT	The following support services should be available: a Interpreters b Social work c Play specialist d Hospital teacher (in-patient care only) e Child psychologist f Dietician	Details of services available *Note: These services may be hospital or community/primary care based. They should be able to provide a timely response to the needs of patients with haemoglobinopathies.*
18 LHT SH	A service agreement for support from community services should be in place. This service agreement should cover, at least: a Guidelines for involvement of community paediatric services in the care of patients with haemoglobinopathies b Role of community services c Exchange of information between hospital and community services and vice versa d Arrangements for liaison with schools.	Service agreement with relevant community services. *Note: Where community and hospital services are managed by the same Trust an agreement covering these issues is still required.*
19 LHT SH	A nurse with competency in cannulation, starting and supervising a transfusion should be available at all times at which children are attending for transfusion.	Details of staff availability Evidence of competences of nursing staff. *Note: Each service should have a method of regularly assuring the competence of nursing staff in cannulation, starting and supervising transfusions. This may be through external training or in-house assurance of competence. Details of the system used, the frequency of updating, the nurses who have reached this level of competence and staffing rotas will be needed to demonstrate compliance with this standard.*
20 LHT SH	All staff involved in the care of children and young people with haemoglobinopathies should undertake regular child protection training.	Details of training undertaken for core members of LHT / SHT.
CLINICAL and REFERRAL GUIDELINES NB. All clinical and referral guidelines should be based on the 'Standards for the Clinical Care of Children and Adults with Beta Thalassaemia in the UK' and 'Sickle Cell Diseasse in Childhood: Standards and Guidelines for Clinical Care.'		
21 LHT SH	Guidelines should be in use covering a How to establish and confirm diagnosis b Parent and sibling testing	Clinical guidelines
22 LHT SH	Clinical guidelines should be in use covering: a Recommended immunisations b Immunisations, other prophylaxis and travel advice prior to travel abroad. c Penicillin prophylaxis while awaiting clarification of diagnosis (sickle cell disease only)	Clinical guidelines *Note: The LHT clinical guidelines should have been agreed with the SHT to which patients are usually referred.*

Ref	Quality Requirement	Demonstration of Compliance
23 LHT SH	Clinical guidelines should be in use covering possible acute presentations including, at least: **For patients with sickle cell disease:** a Fever and infection including major sepsis b Acute pain c Acute anaemia d Stroke and other acute ischaemic events e Acute chest syndrome f Acute splenic sequestration g Abdominal pain / jaundice h Priapism i Changes in vision, including urgent referral for an ophthalmologic opinion j Indications for 'top-up' and for exchange transfusion and practical protocol for undertaking exchange transfusion **For patients with thalassaemia:** a Fever and infection including major sepsis b Unexpected cardiac, hepatic, endocrine decompensation. These guidelines should ensure that patients are transferred to the paediatric ward for assessment as quickly as possible	Clinical guidelines *Note: Teams treating only patients with sickle cell disease or only patients with thalassaemia need guidelines relating to that group of patients.* See also QR 33

Ref	Quality Requirement	Demonstration of Compliance
24 LHT SH	Clinical guidelines should be in use covering routine out-patient monitoring and management between formal annual progress review visits, including: **All patients:** a General assessment of well-being including school attendance b Any difficulties adhering to treatment or other difficulties with care c Monitoring growth and development d Checking for palpable spleen **Patients with sickle cell disease:** e Discussion to ensure analgesics available for home use understood and effective f Informal assessment of cognitive function, learning and behavioural difficulties, including referral if needed g Checking for history of priapism in boys h Checking for and management of nocturnal enuresis i Checking all necessary immunisations up to date j Penicillin therapy and alternative therapy for children who are allergic to penicillin k Monitoring of oxygen saturation by pulse oximeter l demonstrating to parents / carers how to check for splenic enlargement m Monitoring of Hb levels, renal function tests, liver function tests n Indications for early referral to specialist haemoglobinopathy team (LHT only) **Patients with thalassaemia and regularly transfused sickle cell:** a Checking adherence specifically to chelation therapy and any difficulties b Monitoring Hb levels, iron levels, liver function and other biochemistry c Indications for early referral to specialist haemoglobinopathy team	Clinical guidelines Part c is for LHT only

Ref	Quality Requirement	Demonstration of Compliance
25 SHT	Clinical guidelines should be in use covering annual specialist review visits including, at least: **All patients:** a Regularity of school attendance and reasons for absence b Any difficulties adhering to treatment or other difficulties with care c Monitoring growth and development, including review of centile charts d Health promotion and healthy lifestyle advice and support e Contraception and sexual health in relevant age group f Travel advice g Review Hb levels, renal and liver assessment, other biochemistry h Hepatitis B vaccination i Monitoring of hepatitis B antibodies and action to be taken should levels fall j Monitoring for hepatitis C in transfused patients k Discussion and preparation of child for any planned surgery l Indications for consideration of splenectomy m Preparations for splenectomy including recommended immunisations n Treatment of complications of splenectomy, including persistent thrombocytosis. **Patients with sickle cell disease:** a As QR 24 plus b Monitoring and screening for neurological complications, including transcranial Doppler ultrasonography c Indications for imaging to assess the extent of cerebrovascular disease d Indications for overnight oxygen saturation monitoring (sleep study) e Indications for echocardiography including possibility of pulmonary hypertension **Patients with thalassaemia:** a As QRs 31, and 32 where applicable [thalassaemia intermedia] plus b Review annual red cell consumption c Review adequacy and appropriateness of iron chelation regimen d Consideration of options for helping children, young people and their families to adhere to chelation therapy e Audiometry and ophthalmology check for those on desferrioxamine, from age 10 f Cardiological assessment (from age 10) g Testing for endocrine abnormalities (from age 10) h Bone mineral density assessment (from age 10).	*Review protocol* *Notes:* *1 The guidelines should be clear about the arrangements for multi-disciplinary review and involvement of members of the LHT / SHT.* *2 The guidelines should ensure that the care of all patients is reviewed at least annually.* *3 According to local network agreements, some aspects of care review can take place at the LHT and be communicated to SHT in time for the annual review visit* *4 Other aspects, not covered by LHT, should be covered by SHT at review visit.*

Ref	Quality Requirement	Demonstration of Compliance
26 LHT SHT	Guidelines should be in use for referral of patients and their families to a clinical psychologist with experience in the care of patients with haemoglobinopathies (including the option for self-referral)	Clinical guidelines
27 LHT SHT	Guidelines for referral for consideration of bone marrow transplantation should be in use.	Clinical guidelines
Quality Requirements 28 to 33 apply only to teams caring for patients with thalassaemia and / or patients with sickle cell disease who need regular transfusions		
28 LHT SHT	Clinical guidelines should be in use covering: a Indications for regular transfusions b Investigations and vaccinations prior to first transfusion c Monitoring of haemoglobin levels	Clinical guidelines
29 LHT SHT	Clinical guidelines should be in use covering review by a specialist nurse or doctor prior to transfusion to ensure that each transfusion is appropriate.	Clinical guidelines
30 LHT SHT	A Transfusion Policy should be in use covering: a Area/s where transfusions will usually be given b Procedures for checking blood c Staff allowed to undertake cannulation d Recommended number of cannulation attempts e Maximum rate and volume of transfusion according to size of child f Monitoring the transfusions g Management of transfusion reactions h Arrangements for medical cover during transfusion i Arrangements for ensuring that a nurse with appropriate competences is in attendance throughout the transfusion.	Transfusion Policy *Notes:* *1 Only medical staff and nurses with appropriate competences (QR19) should be allowed to undertake cannulation.* *2 Both Standards documents recommend that no more than three cannulation attempts should be made by one individual.* *3 Blood transfusions should be monitored and reactions managed according to the latest British Committee for Standards in Haematology guidelines.* *4 The policy should ensure that patients do not usually wait for more than one hour for cannulation and setting up of the blood transfusion.*
31 LHT SHT	Clinical guidelines for chelation therapy and monitoring iron load should be in use including: a Indications for starting chelation b Choice of regime c Dosage and dosage adjustment d Clinical assessment of tissue damage e Monitoring of serum ferritin f Use of non-invasive estimation of organ-specific iron loading heart and liver by T2*/R2 g Management of side effects of chelators.	Clinical guidelines *Notes:* *1 Starting chelation, and most alterations in treatment regimen, should be discussed with the SHT before change by the LHT.* *2 The LHT clinical guidelines should have been agreed with the SHT.* *3 Guidelines should encourage patient and family involvement in monitoring wherever possible*

Ref	Quality Requirement	Demonstration of Compliance
32 LHT SHT	Clinical guidelines for the management of thalassaemia intermedia should be in use including: a Indications for transfusion b Monitoring iron loading c Indications for splenectomy.	Clinical guidelines *Notes:* *1 This QR may be met by covering specific management issues around thalassaemia intermedia within QR28.* *2 This QR is not applicable to teams treating only patients with sickle cell disease.*
33 LHT SHT	Clinical guidelines should be in use covering: a Indications for exchange transfusion b Arrangements for carrying out an exchange transfusion.	*Clinical guidelines*
SERVICE ORGANISATION and LIAISON WITH OTHER SERVICES		
34 LHT SHT	Clinical guidelines for acute and out-patient monitoring and management (QR23and QR24) should be available and in use in appropriate areas including A&E, clinic and ward areas.	Guidelines available in appropriate clinical areas. *Note: Guidelines may be available in paper and / or electronic forms.*
35 LHT SHT	A protocol should be in use covering the initial clinic visit for patients with haemoglobinopathies covering, at least: a Giving each patient information relevant to their condition (QR1) b Giving each patient their patient-held record (QR4) c Allocation of a named contact for queries and advice to each patient. d Discussion of arrangements for future treatment and care e Sending the GP information relevant to their patient's condition (QR2)	Written protocol *Notes:* *1 Arrangements for future treatment of care should include discussion of care at a LHT closer to the patient's home.* *2 For children, the discussion will involve the parents as well as the child.* *3 This QR is linked with QR39.*
36 LHT SHT	A protocol should be in use covering the initial clinic visit for patients previously treated outside the UK, including: a Full medical history and examination b Investigations c Referral to other specialist services (QR15) d All aspects of QR28	Written protocol
37 SHT	A protocol should be in use covering arrangements for care between SHT and LHT for ongoing care. This protocol should ensure that, to facilitate effective shared care: a All patients have an up to date patient held record and details of their care plan. b The LHT and the patient's GP have received details of the patient's care plan.	Written protocol *Note: The patient's care plan may be part of the patient-held record, be covered in clinic letters or can be a separate document.*

Ref	Quality Requirement	Demonstration of Compliance
38 LHT SHT	A protocol should be in use covering: a Updating patient-held records b Offering patients a permanent record of consultations at which changes to their care plan are discussed. c Recording changes of key contact d Giving further information (QR1) as patients' and families' needs change	Written protocol *Notes:* *1 The permanent record of consultations at which changes to care plans are discussed may be achieved through updating the patient-held record or may involve additional communication.* *2 This QR relates to the LHT / SHT's internal arrangements. It should be consistent with the policy for communication between teams (QR39).*
39 SHT	The SHT and its linked LHTs should have agreed a policy on the communication of clinical information, management plans and important decisions regarding treatment between clinical teams. This protocol should cover information from specialist clinic visits as well as contacts with SHT / LHTs. The protocol should be specific about frequency / indications for communication with the patient's GP	Policy agreed with referring LHTs. *Note: Both Standards documents recommend that communication to the GP should be at least every 6 months and when there are new problems or treatment changes.*
40 LHT SHT	An operational policy should be in use covering: a Teaching children, young people and their patients how to set up an administer subcutaneous desferrioxamine infusions b Encouraging children to participate in setting up and administering their own infusion c Regular assessment and updating administration techniques d Recording of assessments of administration techniques	Operational policy *Note: this QR applies only to teams treating patients with thalassaemia and / or patients with sickle cell disease who require regular transfusion and are receiving desferrioxamine infusions .* *The policy should specify involvement of play specialists, hospital teaching staff, social workers, and clinical psychology in encouraging involvement in setting up and administration of chelation therapy and improving adherence to therapy.*
41 LHT SHT	Patients and families should have choice of attending for blood tests, clinic appointments and blood transfusions 'out of hours' to minimise disruption to normal life	*Details of arrangements*
42 LHT SHT	A protocol should be in use covering: a Follow up of children who do not attend b Communication and follow up of children who move to another area	Written protocol

Ref	Quality Requirement	Demonstration of Compliance
43 SHT	A protocol should be in use covering transition to adult care. This should ensure: a Age guidelines for timing of the transfer. b Involvement of the young person in the decision about transfer. c Involvement of primary health care, social care and adult services in planning the transfer. d Allocation of a named coordinator for the transfer of care. e A preparation period and education programme relating to transfer to adult care. f Communication of clinical information to the adult services. g Arrangements for monitoring during the time immediately after transfer to adult care.	Protocol agreed with adult services to which patients are usually transferred.
44 LHT SHT	The team should have in place: a Mechanisms for receiving feedback from patients and carers about the treatment and care they receive. b Mechanisms for involving patients and carers in decisions about the organisation of the services. c Mechanisms for encouraging the development of local support groups.	Description of current arrangements. Examples of changes made as a result of feedback from patients and carers. Details of local support groups *Note: The arrangements for receiving feedback from patients and carers may involve surveys, focus groups and/or other arrangements. They may be part of Trust-wide arrangements so long as issues relating to haemoglobinopathy services can be identified.*
45 SHT	The SHT should run a programme of training and awareness of the management of patients with haemoglobinopathy for its main referring LHTs.	Details of training and awareness programme
46 LHT	Staff from the LHT should participate in the training and awareness programme run by the SHT to which patients are usually referred.	Details of participation in training and awareness programme.
47 SHT	The SHT should meet at least annually with its referring LHT teams to: a Identify any changes needed to network-wide policies, procedures and guidelines b Review results of audits undertaken c Review any critical incidents including those involving liaison between teams d Consider the content of future training and awareness programmes (QR45)	Evidence of review meeting/s having taken place. *Note: Meetings may be with referring teams together or separately.*
48 LHT	A representative of the LHT should attend each review meeting with the SHT to which patients are usually referred (QR47).	*Evidence of attendance at meetings with main SHT.*

Ref	Quality Requirement	Demonstration of Compliance
49 SHT	The SHT should meet at least annually with representatives of the neonatal screening programme to review progress, identify issues of mutual concern and agree action.	Notes of liaison meetings.
DATA COLLECTION AND AUDIT		
50 LHT SHT	The LHT / SHT should have audited compliance with key standards including: **Patients with sickle cell disease:** a Proportion of patients taking regular penicillin b Proportion of patients fully immunised against pneumococcus c Proportion of patients (HbSS and HbSβ0) who have had Transcranial Doppler ultrasonography undertaken within the last year d Proportion of patients who have had their annual multi-disciplinary review within the last year e Effectiveness of action to contact families who have not attended for follow up appointments. f Review of the care of any patients who have died. **Patients with thalassaemia:** a Proportion of patients on chelation therapy b Proportion of patients who have had their annual multi-disciplinary review within the last year c Adequacy of recording of: • Pre-transfusion Hb levels • Regular monitoring of iron level • Complications of iron overload • Height / weight progression • Spleen size • Support for home chelation programme (QR40) d Effectiveness of action to contact families who have not attended for follow up appointments. e Review of the care of any patients who have died.	*Results of audit undertaken* *Mortality review procedure*
51 SHT and LHT	Data should be systematically entered on all patients, following patient / parental consent, onto the National Haemoglobinopathy Registry.	Record of number of patients from the site entered onto NHR.

Ref	Quality Requirement	Demonstration of Compliance
COMMISSIONERS OF SERVICES		
52	Each Specialist Commissioning Group should have agreed the location of services for its population: a Specialist Haemoglobinopathy Team/s for children and young people b Local Haemoglobinopathy Team/s for children and young people c The expected referral patterns to each SHT and LHT. d The type of patients (sickle cell and / or thalassaemia) who will be treated by each team.	Agreed configuration of services and expected referral patterns. *Notes:* *1 SHTs and LHTs may be located within or outside the area served by the SCG.* *2 Individual children and young people may be referred to Teams other than those specified for clinical reasons, ease of access or patient choice.*
53	Each Specialist Commissioning Group should have: a Compared the staffing, support services and facilities of each SHT and LHT located within its area (QR 52) with the levels expected in QRs 7 to 19. b Agreed a plan for the development of SHTs and LHTs located within its area. c Monitored achievement of the agreed plan at least annually. The agreed development plan should ensure that QRs 7 to 19 are met within 2 to 5 years.	Review of current services. Agreed strategic development plan *Notes:* *1 SHTs may take referrals from more than one Specialist Commissioning Group area. If so, the development plan should be agreed with the main referring Specialist Commissioning Groups.* *2 This QR aims to ensure that each SHT and LHT has a development plan agreed with its main commissioners. This does not replace the individual discussions between commissioning organisations and service providers. All commissioners will be expected, however, to work within the agreed development plan.*

[3]The structure of Specialist Commissioning Groups is currently subject to review. These Quality Requirements apply to whichever organisation has the responsibility for coordinated commissioning of services for patients with haemoglobinopathies.

Extract from 'NHS Sickle Cell and Thalassaemia Screening Programme: Standards for the linked Antenatal Newborn Screening Programme' November 2006, NHS Antenatal and Newborn Screening Programmes

	NEWBORN PROGRAMME OBJECTIVES	CRITERIA	STANDARDS		Level of reporting
			Minimum (Core)	Achievable (Developmental)	
P3	Timely communication of positive screening results (sickle cell disorder) – including a review of parental results	Time by which affected baby results are communicated to parents	90% of sickle cell screening results communicated to parents by four weeks of age	95% of sickle cell screening results communicated to parents by four weeks of age	Audit by clinical network/newborn laboratory catchment area/ named health professional
P4	Effective follow-up of infants with positive screening results (sickle cell disorder) – all babies to be registered with a local clinic/centre (or clinic working as part of clinical network)	Timelines of notification and follow-up of infants with positive screening results Completeness of infants with a positive screening result followed up and registered	95% of parents of infants with a positive screening result notified in person by nominated health care professional by four weeks of age 90% registered with designated/named clinic by eight weeks of age 90% attend local clinic by three months of age	95% of parents of infants with a positive screening result notified in person by nominated health care professional by four weeks of age 95% registered with clinic by eight weeks of age 95% attend local clinic by three months of age	Specialist Clinical networks/named health professional/ specialist laboratory catchment – collated nationally by SC&T Programme Centre
P5	Timely confirmation of diagnosis for infants with a positive screening result**	Diagnostic confirmation of newborn screening results	90% of cases of Hb SS and Hb SC have confirmation of result documented in clinical notes by six months of age Ω	95% of cases of Hb SS and Hb SC have confirmation of result documented in clinical notes by six months Ω	

** Specified conditions: Hb-SS, Hb-SC, Hb-SDPunjab, Hb-SβThalassaemia (β+, β0, δβ, Lepore), Hb-SOArab, Hb-S/HPFH

Ω Due to the small numbers of other conditions, these have not been mentioned here specifically.

	NEWBORN PROGRAMME OBJECTIVES	CRITERIA	STANDARDS		Level of reporting
			Minimum (Core)	Achievable (Developmental)	
	Organisation/ Structure				
S1i	Failsafe to ensure ongoing care	Failsafe policies in laboratories and clinical networks to check if all children with a positive screening result (Sickle Cell Disorder) attend for follow up and act where they do not	Failsafe arrangements in all areas for follow-up and notification and review of non-attendance after one visit for children with a positive screening result (Sickle Cell Disorder)	Less that 5% of cases on registers lost to follow up within the past year	National programme oversight to monitor the overall outcome of the programme
S1ii	Up-to-date registers maintained of babies (cases) for which units are responsible	Specialist clinical networks to have explicit systems for review and follow-up action on cases not attending which include maintaining a register	Less that 10% of cases on registers who have been lost to follow up within the past year		System for reporting of sentinel and adverse events nationally to learn lessons. Developed as part of the clinical networks

Appendix 10 - Standards and guidelines for TCD scanning of children with sickle cell disease

PLEASE NOTE THE FOLLOWING GUIDANCE ISSUED OCTOBER 2010 AFTER PUBLICATION OF THESE TCD STANDARDS & GUIDELINES IN MARCH 2009.

The American STOP trial categories were based on non-imaging TCD and some studies have suggested that TCDi gives blood velocity values up to 10% lower. Therefore children with TCDi velocities >180cm/s but <200cm/s should be assessed very carefully for evidence of cerebrovascular disease. This may include frequent repeat TCD imaging, MRI/MRA or repeat scanning with non-imaging TCD. Regular transfusions may be appropriate in this group if there is evidence of established or progressive cerebrovasculopathy or other neurocognitive concerns. The course of action in these cases must be decided by the clinicians responsible for the clinical care of the child, taking into account individual circumstances and the diagnostic facilities available.

Further work is being undertaken to resolve the apparent discrepancies between the velocities measured by imaging and non-imaging TCD scanning and to harmonise the results from the two techniques.

Organization of TCD scanning services

All children and young adults with sickle cell anaemia (Hb SS) and HbS ß zero thalassaemia, should be offered annual TCD scans from age 2 years until at least age 16 years. The need for children with other types of sickle cell disease to be screened should be reviewed on a case by case basis.

TCD or TCD imaging (TCDi) are both acceptable techniques for performing scanning, with the method of choice depending on local circumstances.

It is expected that the mode of delivery of the service and choice of equipment will depend on the configuration of clinical services for children with sickle cell disease. This will probably be determined by the prevalence of the condition in any particular area. Children could be scanned in an outpatient clinic environment, ultrasound department or in the home. There should be a lead clinician taking responsibility for directing the TCD scanning services within any particular locality.

All parents/carers should be given a verbal explanation of the TCD scanning process and limitations of the procedure, together with an explanation of the follow up process if an abnormality is found. The association between high blood velocity in the cerebral arteries and the risk of a stroke should be made clear and hence the purpose of the test. This should be backed up with appropriate written information. Sufficient verbal and written information should be given to enable an informed decision to be made about the desirability of the TCD scan and accepting the consequences of chronic transfusion if an abnormality is detected.

Scanning protocols and follow-up

The protocols for TCD non-imaging scanning and categorisation of results are based on the criteria developed from the first Stroke Prevention Trial in Sickle Cell Anaemia (STOP 1 trial) in the USA. TCD imaging techniques were not investigated in the STOP trials and the recommendations for the imaging protocols have been based on more recent comparison data between the two methods. Because of these limitations, the method of scanning (TCD or TCDi) must be quoted on the report.

Arterial blood velocities must be examined in the distal intracranial internal carotid artery (ICA) and middle cerebral artery (MCA) on both sides of the head. Velocities in the anterior cerebral arteries (ACA) and posterior cerebral arteries (PCA) should also be examined for additional information and to help refine the stroke risk assessment, but are not used in the STOP classification of risk.

The scan results should be divided into five categories depending on the time averaged maximal mean (TAMM) velocity recorded, whether in the ICA or MCA or the bifurcation of the two arteries:

- Inadequate image
- Unusual low velocity
- Normal velocity - 'low risk'
- Borderline velocity - 'conditional'
- High velocity - 'high risk'

A TCD scan would be defined as inadequate if for whatever reason unsatisfactory results were obtained. This might be due to such causes as an uncooperative child (in which case a repeat scan should be considered), poor scanning window (in which case an alternative scanning method such as MRI/MRA should be considered), previous stroke, etc. The time interval for a repeat scan would depend on clinical judgement and considered on a 'case by case' basis.

Low velocities of <70 cm/s in the MCA or a velocity <50% of the contralateral MCA are indicative of possible occlusion and should prompt further investigations with MRI or CT. Assessment of the blood velocities in the ACAs and extracranial ICAs at the time of the TCD scan might provide useful additional information in these cases.

The TAMM blood velocities used as cut-offs to define the risk limits would be:

TCD non-imaging	
Normal velocity - 'standard risk'	<170 cm/s
Borderline velocity - 'conditional'	170 to 199 cm/s
High velocity - 'high risk'	≥200 cm/s

TCDi using duplex scanners can be used to examine children, although some studies have shown that TCDi velocities can be up to 15% lower than those measured by non imaging TCD. Improved technique and a change in imaging parameters can reduce this difference to 10% or less. If TCDi is used as the scanning technique, appropriate allowances should be made for velocities that are within 10% of the conditional or abnormal risk thresholds. (Further work will be undertaken to examine the reasons for these discrepancies and decide whether separate cut-offs are justified.) The (rounded) values for the cut-offs for TCD imaging based on this 10% allowance would be:

TCD imaging	
Normal velocity - 'standard risk'	<155 cm/s
Borderline velocity - 'conditional'	155 to 179 cm/s
High velocity - 'high risk'	≥180 cm/s

Please see guidance note above issued October 2010.

This classification should be based on the maximal velocity recorded during the examination, with appropriate regard to the settings of the scanning equipment. Adequate training should ensure that the optimum reading is taken.

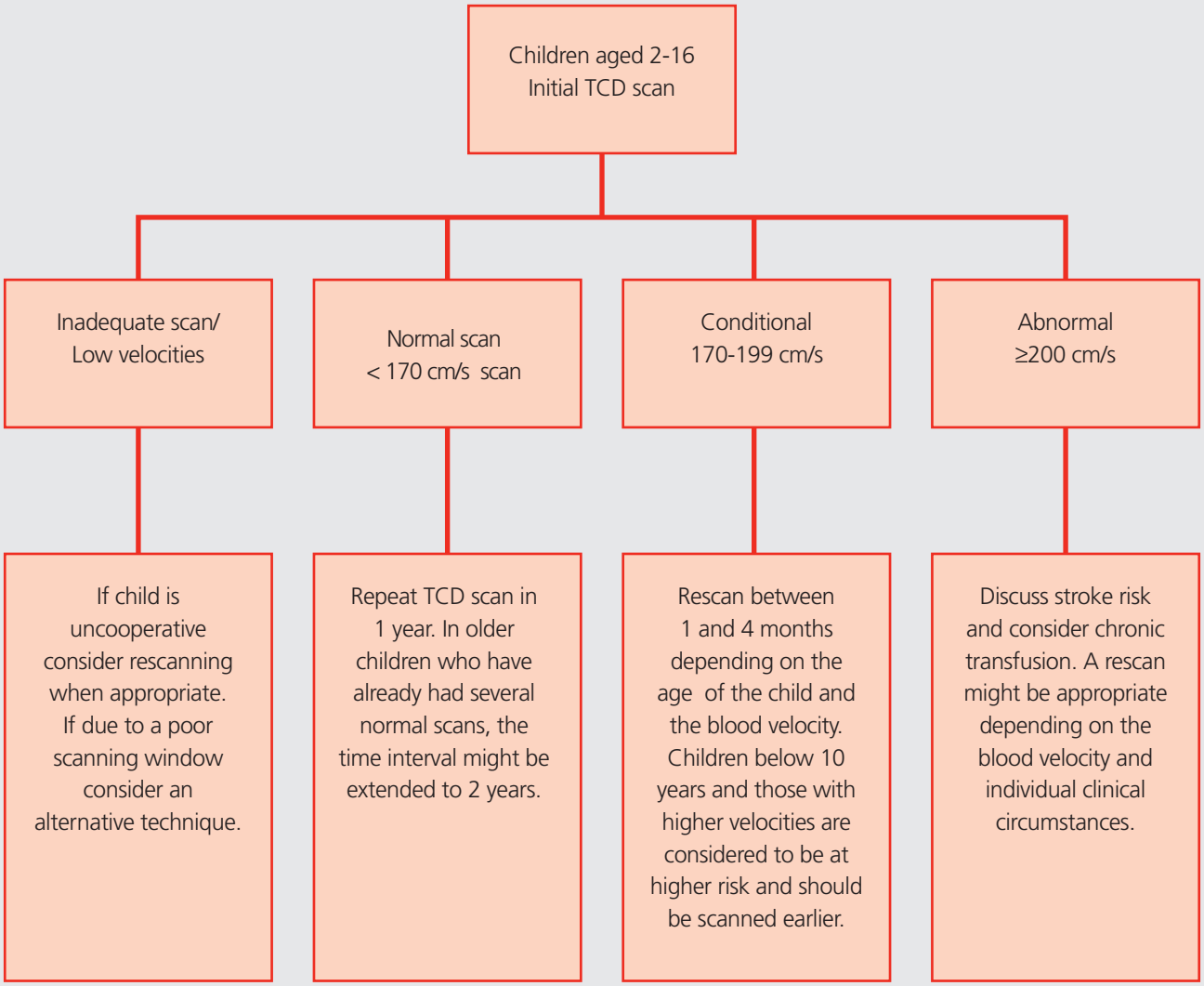
The action taken following the categorisation of results should depend on the age of the child and follow the protocols as given in the associated algorithm. Repeat TCD scans should be undertaken at the time intervals recommended. Because of the long-term consequences of starting chronic transfusions in children at high risk, all available data should be considered prior to beginning treatment. This will include a comprehensive neurological assessment and the results of other imaging studies such as MRI/MRA, although these are not used in the risk classification.

Assessment of extracranial arteries are not used in the formal protocols, but may be used locally to refine a diagnosis and prognosis.

Appropriate magnetic resonance or CT imaging studies to assess the extent of the cerebrovascular disease should be considered if the child is placed in the high risk category requiring blood transfusions, although treatment should not be altered or delayed for this reason.

There will be a need for some TCD scans once a child has started on chronic transfusions to ensure that blood velocities have decreased to acceptable levels. The time intervals for performing these scans will depend on individual clinical circumstances and should be considered on a case-by-case basis.

TCD Scanning Decision-Tree


Children aged 2-16
Initial TCD scan
Inadequate scan/
Low velocities
Normal scan
< 170 cm/s scan
Conditional
170-199 cm/s
Abnormal
≥200 cm/s
If child is uncooperative consider rescanning when appropriate. If due to a poor scanning window consider an alternative technique.
Repeat TCD scan in 1 year. In older children who have already had several normal scans, the time interval might be extended to 2 years.
Rescan between 1 and 4 months depending on the age of the child and the blood velocity. Children below 10 years and those with higher velocities are considered to be at higher risk and should be scanned earlier.
Discuss stroke risk and consider chronic transfusion. A rescan might be appropriate depending on the blood velocity and individual clinical circumstances.

Velocities are TCD non-imaging, time-averaged, maximal scan velocities (TAMMV). Decisions apply to TAMMVs in the distal ICA, bifurcation and/or MCA only. For bilateral or multifocal TAMMVs ≥ 170 cm/s, choose the highest single value for the decision tree. Recurrent inadequate scans or low velocities may indicate severe stenosis. Consider using other imaging techniques. For any particular child, detailed clinical knowledge and judgement might override this picture.

Training

All operators performing TCD or TCDi scanning on children must have had appropriate training in the technique.

Some aspects of training will be organised nationally, incorporating three elements:

- Training day on the theory of TCD scanning, protocols, equipment, etc. with some TCD scanning practice on adults/other trainees.
- Secondment of at least one day for each trainee to a 'centre of excellence' to receive 'hands on' TCD training with children in a clinic environment. Further practice can be carried out locally, but only under adequate supervision in a clinic environment.
- Visit to the trainee's place of work by a tutor to observe their TCD scanning in practice and review traces/images, etc.

Trainees will be expected to carry out specific scanning exercises designed to develop their technique. These can be carried out on adult volunteers at their own centre.

Trainees will be expected to keep a log book showing records of the subjects scanned and the procedures undertaken. It would normally be expected that trainees scan at least 20 children to gain competence in the technique.

When a trainee has demonstrated a thorough understanding of the theoretical and practical aspects of TCD scanning in children, they would be 'signed off' by their line manager (in conjunction with their tutor) as competent to scan unsupervised. The Programme Centre will work towards establishing a national register of practitioners competent in paediatric TCD scanning and a national certificate of competence to practice.

Quality assurance

Those centres undertaking TCD scanning must be part of a network of care for sickle cell children and be part of any national approval/accreditation process of those centres.

TCD scanning should only be performed by those operators seeing a sufficient number of children to enable them to remain proficient in the process. The guideline number of TCD scans to achieve this proficiency is considered to be a minimum of 40 per year. It would be appropriate to consider refresher training if operators performed fewer than this number. Operators performing TCD or similar techniques in other groups of patients might justify fewer than 40 TCD scans on sickle cell children. Network centres must determine the best way to provide sufficient numbers of staff to provide a quality TCD service for the sickle cell population in their area.

The Programme Centre will work towards the establishment of a national quality assurance scheme, whereby a number of scans for each operator will be assessed for their quality by a peer review system. This is likely to be by a process of local peer review within the clinical networks or possibly by submission to an independent central body. Unsatisfactory images will result in a requirement for a further period of training.

The Programme Centre will work towards the establishment of a national database to incorporate all TCD scanning results on children with sickle cell disease. This will enable scanning results to be correlated with clinical outcome and hence audit the effectiveness of the scanning programme. This will also form part of a quality assurance scheme whereby centres might be identified whose TCD results or clinical outcomes differ from their peers.

Appendix 11 - Sickle cell and thalassaemia centres nationally

Greater London

BARKING & DAGENHAM, HAVERING & REDBRIDGE
Haemoglobin Disorders Service
Cedar Centre- Unit Management Office
King George's Hospital, Barley Lane
Goodmayes, Essex IG3 8YB
Tel/Fax: 020 8970 8301

BARTS & THE LONDON NHS TRUSTS
Department of Haematology
Royal London Hospital Whitechapel
London E1 1BB
Tel: 020 7377 7000

BEXLEY & BROMLEY
(See Greenwich)

BRENT
Brent Sickle Cell & Thalassaemia Centre
Central Middlesex Hospital
Acton Lane, London NW10 7NS
Tel: 020 8453 2050 / Fax: 020 8453 2051
Website: www.sickle-thal.nwlh.nhs.uk

CAMDEN & ISLINGTON
Sickle Cell & Thalassaemia Centre
17a Hornsey Street
London N7 8GG
Tel: 020 3316 8853 / Fax: 020 7690 3552

CITY & HACKNEY
Sickle Cell & Thalassaemia Centre
457 Queensbridge Road
Hackney, London E8 3AS
Tel: 020 7683 4570 / Fax: 020 7853 6709

CROYDON
Sickle Cell & Thalassaemia Centre
316-320 Whitehorse Road
Croydon, CR0 2LE
Tel/Fax: 020 8251 7248

EALING
Ealing and Harrow Community Services
Featherstone Road Clinic
Hartington Road, Southall
Middlesex, UB2 5BQ
Tel: 020 8383 5446/5454 / Fax: 020 8843 1482

GREENWICH & BEXLEY
Sickle & Thalassaemia Service
Gallions Reach Health Centre
Bentham Road, Thamesmead SE28 8BE
Tel: 020 8320 5712/3 / Fax: 020 8311 8895

HAMMERSMITH & FULHAM PCT
Sickle & Thalassaemia Service
Richford Gate Primary Care Centre
Richford Street, London W6 7HY
Tel: 020 8237 2980 / Fax: 020 8237 2986

HAMMERSMITH HOSPITAL
London Borough of Hammersmith & Fulham
Physical Disabilities Team, 2nd Floor
145 Kings Street, London W6 9XY

HARINGEY
George Marsh Sickle & Thalassaemia Centre
St Ann's Hospital (part of North Middlesex University
Hospital NHS Trust)
St Ann's Road, Tottenham
London N15 3TH
Tel: 020 8442 6230 / Fax: 020 8442 6575

HOUNSLOW & RICHMOND
3rd Floor, Heart of Hounslow Centre for Health
92 Bath Road
Hounslow TW3 3LN
Tel: 020 8630 3363 / Fax: 020 8630 3380

NEWHAM
The Sickle & Thalassaemia Centre
19 –21 High Street South
East Ham, London E6 6EN
Tel: 020 8821 0800 / Fax: 020 8821 0808

SOUTH EAST LONDON
Sickle Cell & Thalassaemia Centre, Wooden Spoon House
5 Dugard Way, Off Renfrew Road
Kennington, London SE11 4TH
Tel: 020 3049 5993 / Fax: 020 3049 6069

TOWER HAMLETS
Sickle Cell & Thalassaemia Service
9-11 Brick Lane, Spitalfields
London E1 6PU
Tel: 0207 247 8251 / Fax: 0207 247 2661

WALTHAM FOREST
Outer North East London Community Services (ONELCS)
Sickle & Thalassaemia Centre, Wood Street Health Centre
6 Linford Way, Walthamstow
London E17 3LA
Tel: 020 8430 7639 / Fax: 020 8430 7641

WANDSWORTH
Sickle Cell & Thalassaemia Counselling & Information Service
Balham Health Centre
120 Bedford Hill
Balham, London SW12 9HP
Tel: 020 8700 0615 / Fax: 020 8700 0615

Centres outside London

AIREDALE (WEST YORKSHIRE)
Keighley Health Centre
Oakworth Road, Keighley
West Yorkshire BD21 1SA
Tel: 01535 606 111

BIRMINGHAM COMMUNITY
Birmingham Sickle Cell & Thalassaemia Service
Soho Health Centre, Soho Road
Handsworth
Birmingham B21 9RY
Tel: 0121 545 1655 / Fax: 0121 241 6736

ACUTE
Sandwell & West Birmingham NHS Trust (Acute & Counselling)
Sickle Cell & Thalassaemia Centre
City Hospital, Dudley Road
Winson Green, Birmingham B18 7QH
Tel: 0121 507 6040 / Fax: 0121 507 6050

BRADFORD
Sickle Cell & Thalassaemia Department
Manningham Clinic, Lumb Lane
Bradford BD8 7SY
Tel: 01274 730 836

BRISTOL
Sickle Cell and Thalassaemia Service
Bristol Community Health, Level 6, South Plaza
Marlborough Street
Bristol BS1 4NX
Tel: 0117 900 2204 / Fax: 0117 900 2201

CARDIFF
Sickle & Thalassaemia Centre
Butetown Health Centre
Loudoun Square, Butetown
Cardiff CF10 5UZ
Tel: 02920 471 055 / Fax: 02920 482 674

COVENTRY
Sickle Cell & Thalassaemia Service
Coventry & Warwickshire Hospital Site
Stoney Stanton Road
Coventry CV1 4FH
Tel: 024 7624 6551

DERBY (SOUTH)
Haematology Department
5th Floor, Derby City General Hospital
Uttoxeter Road
Derby DE22 3NE
Tel: 01332 788 512

DUDLEY
Netherton Health Centre
Halesowen Road, Netherton
Dudley DY9 9PU
Tel: 01384 366 500

EAST BERKSHIRE
(Slough, Windsor, Ascot, Maidenhead)
Specialist Practitioner (sickle cell and thalassaemia)
Berkshire East PCT
Upton Hospital, Cedar House
Slough, Berkshire SL1 2BJ
Tel: 01753 635 491 / Fax: 01753 635 291.

EAST LANCASHIRE AND CUMBRIA AREA
Haemoglobinopathy Specialist Practitioner
Burnley General Hospital
Casterton Ave
Burnley BB10 2PQ
Tel: 01282 804 487

ESSEX
Advanced Specialist Practitioner for Sickle Cell & Thalassemia
St Clements Health Centre, London Road
West Thurrock, Grays
Essex RM20 3DR
Tel: 01708 895 472 / Fax: 01708 895 476

GLOUCESTER
Sickle & Thalassaemia Centre, The Edward Jenner Clinical Unit
Gloucestershire Royal Hospitals Foundation NHS Trust
Greater Western Road
Gloucester GL1 3NN
Tel: 08454 225 224 / Fax: 08454 225 273

HUDDERSFIELD
Princess Royal Community Health Centre
Greenhead Road
Huddersfield HD1 4EW
Tel: 01484 344 321

HULL
Newington Healthcare Centre
Plane Street
Hull HU3 6BY
Tel: 01482 344 209

LEEDS
Sickle & Thalassaemia Centre, Chapeltown Health Centre
Spencer Place
Leeds LS7 4BB
Tel: 0113 295 1000 / Fax: 0113 295 1018

LEICESTERSHIRE
Sickle Cell & Thalassaemia Service
The Merlyn Vaz Health & Social Care Centre
1 Spinney Hill Road
Leicester LE5 3GH
Tel: 0116 294 3010 / Fax: 0116 294 3058

LIVERPOOL
Centre for Inherited Blood Disorders (Sickle Cell, Thalassaemia and G6PD Deficiency)
Abercromby Health Centre
Grove Street
Liverpool L8 6JJ
Tel: 0151 708 9370

LUTON
Sickle Cell & Thalassaemia Service, NHS Luton Community Services
The Lodge
4 George Street West
Luton LU1 2BJ
Tel: 01582 708 312 / Fax: 01582 511 001

MANCHESTER
Sickle & Thalassaemia Centre
352 Oxford Road, At Junction of Denmark Road
Manchester M13 9NL
Tel: 0161 274 3322 / Fax: 0161 273 7490

MILTON KEYNES
Sickle & Thalassaemia Service
Milton Keynes Community Health Services
Whalley Drive Clinic, Whalley Drive Bletchey
Milton Keynes MK3 6EN
Tel: 01908 650 418

NOTTINGHAM
Nottingham Sickle Cell and Thalassaemia Service
The Mary Potter Centre in Hyson Green
Gregory Boulevard, Hyson Green
Nottingham NG7 5HY
Tel: 0115 883 8424 / Fax: 0115 883 8425

PRESTON
Sickle & Thalassaemia Service
Saul Street Clinic
Saul Street
Preston PR1 2QU
Tel: 01772 401185 / Fax: 01772 883 502

READING (WEST BERKSHIRE)
Sickle & Thalassaemia Service
Haematology Department, Royal Berkshire Hospital
London Road
Reading, Berks RG1 5AN
Tel: 0118 322 7292 / Fax: 0118 322 7755

SCOTLAND (WEST of SCOTLAND)
Sickle & Thalassaemia Genetic Counselling Service
Ferguson-Smith Centre for Clinical Genetics
Regional Genetic Service, Yorkhill Hospital
Glasgow, Scotland G3 8SJ
Tel: 0141 201 0808 (reception) / Fax: 0141 201 0361

SHEFFIELD
Haemoglobinopathy Service
Sheffield Children's Hospital, Room E61, Orange Wing
Western Bank
Sheffield S10 2TH
Tel: 0114 271 7707 / Fax: 0114 226 0640

SOUTHAMPTON
Sickle & Thalassaemia Service
Newtown Health Clinic
24-26 Lyon Street
Southampton SO14 0LX
Tel/Fax: 02380 900 222

WALSALL
Acute
Sickle Cell & Thalassaemia Service
Pathology Department, Manor Hospital
Moat Road, Walsall
West Midlands WS2 9PS
Tel: 01922 721 172 / Fax: 01922 656 809
Community
Haemoglobinopathy service
Bentley Health Centre, Churchill Road
Walsall WS2 0AW
Tel: 01922 423 506/07

WEST MIDLANDS PERINATAL INSTITUTE
Crystal Court, Aston Cross
Birmingham B6 5RQ
Tel: 0121 687 3471 / Fax: 0121 687 3401

WOLVERHAMPTON
Sickle Cell & Thalassaemia Support Project
2nd Floor Office, St John's House
St John's Square
Wolverhampton WV2 4BH
Tel: 01902 444 076/77 / Fax: 01902 445 322
Website: www.sctsp.org.uk

NHS Sickle Cell and Thalassaemia Screening Programme

Division of Health and Social Care Research
King's College School of Medicine
Tel 020 7848 6634
Fax 020 7848 6620
Email : haemscreening@kcl.ac.uk
Website: www.sct.screening.nhs.uk

Sickle Cell Society

54 Station Road
London NW10 4UA
Tel 020 8961 7795
Fax 020 89618346
Email info@sicklecellsociety.org
Website: www.sicklecellsociety.org

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